UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

TXR No. 0051925

June 6, 2003

MEMORANDUM

SUBJECT: **OXADIAZON**. Response to the 60-day Comments on the HED Chapter of the Reregistration Eligibility Decision Document (RED). PC Code: 109001, Case # 819425, Submission No. S635115, DP Barcode D290005

FROM: Nancy E. McCarroll, Toxicologist/Risk Assessor
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THRU: Alberto Protzel, Ph.D., Branch Senior Scientist
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Health Effects Division (7509C)

TO: Mark Seaton, Chemical Review Manager
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Special Review and Reregistration Division (7508W)

Comments received from the registrant, Bayer Environmental Science (formerly, Aventis Environmental Science) on the Human Health Risk Assessment for the reregistration of Oxadiazon have been addressed in the revised HED Chapter of the RED. The revised document is attached and the revisions are as follows:

cc: Susan Makris, HED
Margaret Rice, SRRD

Actions in Response to Bayer's 60-Day Comments (Report dated April 17, 2003)

I GENERAL COMMENTS

Global Change Throughout the Document

RESPONSE: At the request of the registrant, the names "Aventis Enviromental Science" and "Aventis" have been changed throughout the Toxicology, Occupational and Residential Exposure and Chemistry chapters and Health Effects Division's (HED's) Risk Assessment Chapter of the Reregistration Eligibility Decision (RED) document on Oxidazion and now read "Bayer Enviromental Science"or "Bayer", respectively.

II COMMENTS ON TOXICOLOGY ISSUES

a. Lack of Agreement with the Carcinogenicity Peer Review Committee's (CARC) classification of Oxadiazon as "Likely to be Carcinogenic to Humans" because Oxadiazon is a peroxisome proliferator.

Bayer disagrees with the CARC's classification of Oxadiazon as a "Likely to be Carcinogenic to Humans" because the registrant believes that "the available evidence indicates that Oxadiazon belongs to the peroxisome proliferator class of compounds.

RESPONSE: Based on the weight-of-the-evidence, the HED's Mechanism of Toxicity Assessment Review Committee (MTARC), which convened on Feburary 8, 2001, concluded that Oxadiazon was not genotoxic. Based on the findings from a 14-day oral mechanistic study in rats (MRID No. 42310001)[1] and data from a journal article (*Richert et al., 1996*)[2] that was found and extracted by our reviewers, MTARC concluded that owing to shortcomings in the database, the above additional pieces of information do not convincingly support peroxisome proliferation as the non-genotoxic mode of action for Oxadiazon. The reasons for this decision were outlined in the Memorandum of Feburary 28, 2001[3] and are listed below:

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[1] S.C. Price (1991). Studies on Morphological and Biochemical Changes in the Livers of Rats Treated for 14 Days with Oxadiazon. Robens Institute of Health and Safety, Surrey, England; Study No. R190/0312; Report dated January 9, 1991(Unpublished) MRID No. 42310001.

[2] Richert, L., Price, S., Chesne, C., Maita, K. Carmichael, N. (1996). Comparison of the induction of hepatic peroxisome proliferation by the herbicide oxadiazon *in vivo* in rats, mice, and dogs and *in vitro* in rat and human hepatocytes. Toxicol. Appl. Pharmacol 141: 35-43.

[3] HED Memorandum, Assessment of Mode of Action on Liver Carcinogenicity, February 28, 2001. TXR No. 0050506

1. MTARC follows the guidance and criteria established by the International Life Science Institute (ILSI) for evaluating peroxisome proliferation as a proposed mode of action for non-genotoxic, tumorigenic pesticides. In the case of Oxadiazon, there is ample evidence of increased liver weights in both sexes of several rat strains, two mouse strains and Beagle dogs throughout the database. However, there are no accompanying studies on cell proliferation such as the effect, if any, of Oxadiazon on replicative or scheduled DNA synthesis (SDS) in the liver. Positive *in vivo* data on SDS are necessary to demonstrate that increased liver weight is associated with mitogenic activity and not with cytotoxicity. Additionally, since cell proliferation is linked directly to tumor formation, data on SDS can provide a sensitive endpoint for a possible bench mark dose analysis.

2. MTARC has concerns regarding the lack of concordance between the dose response for peroxisomal enzymatic activity and tumor formation. As stated in the MTARC report, Oxadiazon induced a significant increase in tumors at the lowest dose tested (*e.g*, 10.6 mg/kg/day) in the submitted mouse chronic toxicity and carcinogenicity study (MRID No. 40993301)[4] while *Richert et al., 1996* reported only marginal and nonsignificant activity for peroxisomal palmitoyl CoA oxidase (PPCO) after mice were treated for 14 days with a higher dose (20 mg/kg/day). Similar results were reported in mice for acetyl carnitine transferase (ACT). Additionally, only a slight increase in the number of peroxisomes was seen by *Richert et al., 1996* at 20 mg/kg/day. These findings are of concern because changes such as increased peroxisomal enzymes or increased number and size of perixosomes are necessary steps in tumors formation. Without unambiguous data, the Agency is reluctant to depart from satisfying all of ILSI criteria for peroxisome proliferation. Based on MTARC's experience with peroxisome proliferators, it was further stated, that increased peroxisome enzyme activity generally occurs (regardless of the time interval) at doses near or lower than the tumorigenic doses. This claim is supported by the findings from mechanistic studies with two peroxisomal proliferating pesticides, Lactofen[5] and Acifluorfen[6] but not with Oxadiazon.

3. MTARC continues to have concerns related to the significance of decreased catalase activity reported in the 14-day rat study (MRID No. 42310001). Since catalase activity is a marker enzyme for the peroxisome organelle, it is expected to

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[4] Shirasu, Y. (1987). Oxadiazon-23 Month Oral Chronic Toxicity and Oncogenicity Study in Mice, Institute of Environmental Toxicology, Mitsukaido Laboratories, Tokyo, Japan, Report dated February, 1987 (Unpublished). MRID No. 40993301.

[5] HED Memorandum: Lactofen: Report of the Mechanism of Toxicity Assessment Review Committee, dated March 12, 2001.

[6] HED Memorandum: Mechanism of Toxicity SARC Report: Acifluorfen (PC Code 114402), dated May 14, 2003.

increase 2-fold in the presence of a peroxisome proliferator[7]. This issue was not addressed in the 14-day rat study or in the 60-day comment document prepared by the Registrant.

4. MTARC also believes that studies in mice satisfying all of ILSI's criteria are necessary before the Committee will reconvene to make a determination on Oxadiazon

b. Lack of Agreement with the Carcinogenicity Peer Review Committee's (CARC) classification of Oxadiazon as "Likely to be Carcinogenic to Humans" because humans are not responsive to this class of compounds.

Bayer commented that since Oxadiazon is a peroxisome proliferator and thus a rodent carcinogen with a threshold, it is not likely to present a risk to humans.

RESPONSE: None of the U.S. regulatory agencies, including EPA have developed a policy on whether pesticides that are shown to be rodent peroxisome proliferators have any relevant impact on human health and risk assessments. The Agency is working closely with ILSI on this issue but can not depart from established policy until ILSI has released its final report on peroxisome proliferators. Until that time, the Agency can not rule out the possibility that exposure to peroxisome proliferators negates a human cancer risk. Nevertheless, with compelling data showing that Oxadizon is a peroxisome proliferator (see Response Section II, a) combined with a credible dose response from a sensitive endpoint, the Q_1^* may be removed and the risk unit may be expressed based on a benchmark dose analysis. From the above considerations and in light of the absence of new data, the original conclusion rendered by the MTARC has not changed and is reiterated below:

"The Committee concluded, therefore, that peroxisome proliferation may be a possible mode of action for Oxadiazon-induced liver tumors in rats and mice. However, because of shortcomings in the data base, the available information do not support this proposed non-genotoxic mode of action for Oxadiazon at this time."

c. Data wavier for the 28-day inhalation study

Bayer requested that the 28-day inhalation toxicity data requirement be waived because the fine aerosol particles used in guideline inhalation studies (MMAD of 1-4 μm) have no relevance to aerial spraying with nozzles that produce droplets with a volume median diameter (VMD) ranging from 125-250 μm.

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[7] Cattley, R.C., DeLuca, J., Elcombe, C., Fenner-Crisp, P., Lake, B.G., Marsman, D.S., Pastoor, T.A., Popp, J.A., Robinson, D.E., Schwetz, B., Tugwood, J., Wahli, W. (1998). Do peroxisome proliferating compounds pose a hepatocarcinogenic hazard to humans? Reg Toxicol and Pharm 27:47-60.

RESPONSE: It is a common misconception that the small particle size used in a rodent study (MMAD of 1-3 µm in acute studies, 1-4 µm in multiple exposure studies) has no relevance to the large droplet size that comes from medium to coarse nozzles during spraying. This reasoning, however, cannot be used to justify granting a waiver.

The sprayed VDM to which humans are exposed is far smaller than the nozzle VDM. Pesticides are typically mixed with large quantities of water before spraying. When the aqueous mix is aerially sprayed, droplets rapidly shrink as they fall due to water evaporation. The degree of shrinkage depends on temperature, relative humidity, particle size, and the length of time that the droplets are suspended in the air. A droplet that is 125-250 µm in diameter (*e.g.*, VMD for Ronstar®) when it leaves the nozzle may be considerably smaller when it reaches the ground (perhaps 2-15 µm). Since humans are capable of inhaling particles >100 µm, it is reasonable to expect a significant portion of these particles to be inhaled. While most large particles are captured in the nose, some are capable of reaching the lungs. Large particles have the potential to do considerable local damage if they are absorbed because of the volume of material they contain. HED's waiver criteria state that a product formulation or application method can be considered essentially non-inhalable provided ≥99% of the particles are >100 µm in diameter.

Furthermore, rats have tortuous nasal turbinates that are extremely efficient at removing particles from inhaled air, hence most particles larger than 1-2 µm are captured in the rodent nose. By contrast, human noses are far less efficient at removing particles. Rats are also obligate nose breathers while humans are not, so whatever protection the nose provides is bypassed when humans breathe through their mouths.

The OPPTS Guidelines require an MMAD of 1-3 µm in inhalation toxicity studies of aerosols so that a portion of the test article will reach the lungs. If rats are exposed to larger particles, the lungs will be virtually unexposed. While lung exposure is important, inhalation exposure can involve the entire respiratory tract. Depending on the physical and chemical properties of the active ingredient, absorption and portal-of-entry effects (e.g. irritation, edema, cellular damage, etc.) can occur anywhere from the nose to the alveoli.

These issues were brought to HED's attention in 1991 when the Technical Committee of the Inhalation Specialty Section of the Society of Toxicology challenged HED's acute inhalation limit test and particle size criteria.[8] These issues were presented to the Science Advisory Panel on December 15, 1993. The Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity Studies[9] summarizes the history and the science behind these issues and provides the policy that is still in use today. It describes why using an MMAD of 1-4 µm in acute studies and 1-3 µm in multiple exposure studies is relevant to real world exposure in humans.

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[8] Technical Committee of the Inhalation Specialty Section, Society of Toxicology. **Recommendations for the Conduct of Acute Inhalation Limit Tests**. Fundamental and Applied Toxicology. Volume 18. 1992. Pages 321-327.

[9] John E. Whalan and John C. Redden. **Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity Studies**. Health Effects Division. February 1, 1994. Docket control number OPP-00394.

Based on the above considerations, granting a waiver for sprayed products based on the disparity between laboratory and "real-world" particle sizes would go against HED policy.

d. Typographical error (page 18)

RESPONSE: The typographical error noted by the Registrant (" For the long-term dermal exposure, an oral endpoint was also selected **using a NOAEL of 0.036 mg/kg/day**....") has been corrected to read:

"... using a NOAEL of 0.36 mg/kg/day...."

III. COMMENTS ON WATER ISSUES

a. Estimated drinking water concentration from surface water of 246 μg/L (acute peak value)/ Table 11a

Bayer claimed that the acute surface water concentration of 246 μg/L, calculated with the model FIRST was an overestimation of the likely exposure and also cited Table 11a.

RESPONSE: A Tier II estimated drinking water concentration (EDWCs) assessment performed by the Environmental Fate and Effects Division (EFED)[10] was completed in April 2002 but was not available at the time the preliminary Human Health Risk Assessment or the revised HED Chapter of the Reregistration Eligibility Decision Document (RED) were released. The HED chapter has now been revised to reflect the use of the PRZM/EXAMS modeling and basing the EDWCs for Oxadiazon on the proposed maximum application rate of 8.0 lbs a.i./A and 3 applications to a golf course (constituting the major use of the pesticide). Accordingly, the acute surface water concentration of 246 μg/L, calculated with the model FIRST has been reduced to 181 μg/L.
The refined value has been incorporated into the HED Human Health Risk Assessment (pp. 6, 21, and 41 and Table 11a) and the EFED chapter.

b. Table 11b, Chronic DWLOC Calculations / EDWC from surface water of 100 μg/L is an overestimate

The Registrant claimed that the chronic surface water concentration of 100 μg/L, calculated with the model FIRST was an overestimation of the likely chronic exposure and also cited Table 11b.

RESPONSE: A Tier II estimated drinking water concentration (EDWCs) assessment performed by

[10] EFED Memorandum: Tier II Estimated Drinking Water Concentrations (EDWCs) for Human Health Risk for Oxadiazon on Florida Golf Course, DP Code: D281176, dated April 15, 2002.

the Environmental Fate and Effects Division (EFED)[11] was completed in April 2002 but was not available at the time the preliminary Human Health Risk Assessment or the revised HED Chapter of the Reregistration Eligibility Decision Document (RED) were released. The HED chapter has now been revised to reflect the use of the PRZM/EXAMS modeling and basing the EDWCs for Oxadiazon on the proposed maximum application rate of 8.0 lbs a.i./A and 3 applications to a golf course (constituting the major use of the pesticide). Accordingly, the chronic surface water concentration of 100 μg/L, calculated with the model FIRST has been reduced to 65 μg/L using PRZM/EXAM modeling. Despite this refinement, the chronic DWLOCs for infants and children (36 μg/mL) are still lower than the refined value (65 μg/L). Therefore, HED's conclusion, that there are concerns for children chronically exposed to Oxadiazon in drinking water derived from surface waters, has not changed. The refined values and appropriate text have been incorporated into the HED Human Health Risk Assessment (pp. 6, and 42 and Table 11b) and the EFED chapter.

c. Table 11c, Chronic Cancer DWLOC Calculations / EDWC from surface water of 100 μg/L is an overestimate

The Registrant claimed that the chronic cancer surface water concentration of 100 μg/L, calculated with the model FIRST was an overestimation of the likely chronic exposure and also cited Table 11c.

RESPONSE: A Tier II estimated drinking water concentration (EDWCs) assessment performed by the Environmental Fate and Effects Division (EFED)[12] was completed in April 2002 but was not available at the time the preliminary Human Health Risk Assessment or the revised HED Chapter of the Reregistration Eligibility Decision Document (RED) were released. The HED chapter has now been revised to reflect the use of the PRZM/EXAMS modeling and basing the EDWCs for Oxadiazon on the proposed maximum application rate of 8.0 lbs a.i./A and 3 applications to a golf course (constituting the major use of the pesticide). Accordingly, the chronic cancer surface water concentration of 100 μg/L, calculated with the model FIRST has been reduced to 56 μg/L using PRZM/EXAM modeling. Despite this refinement, the surface water cancer DWLOC for the U.S. population (0.49 μg/L) remains lower than the refined value (56 μg/L). Therefore, HED's conclusion, that there is a concern for lifetime exposure to Oxadiazon in surface and ground water, remains unchanged. The refined values and appropriate text have been incorporated into the HED Human Health Risk Assessment (p. 42, Table 11c) and the EFED chapter.

IV. COMMENTS ON EXPOSURE ISSUES

a. Harmonization within and between documents

Bayer notes that page 5 of the Occupational and Residential Exposure (ORE) document provides a

[11] Ibid

[12] Ibid

use figure on golf courses of 77% while the Environmental Fate and Effects Division (EFED) Risk Assessment uses 77% or 65%. The use figures should be harmonized within and between the different documents.

RESPONSE: This error has been corrected in the revised ORE document.

Bayer also notes that page 8 of the ORE document provides a use figure on golf courses of 71% while the EFED Risk Assessment uses 77% or 65%. The use figures should be harmonized within and between the different documents.

RESPONSE: This error has been corrected to 77% in the revised ORE document.

b. Unacceptability of Transferable Turf Residue (TTR) studies (MRID 44995501 and -02)

Bayer finds the statement and the conclusion on page 27 of the ORE document, to be confusing. The two TTR studies (MRID# 449955-01 and 449955-02) were apparently not accepted by EPA because they used the modified California Roller sampling device and not the ORETF device. Bayer refers the Agency to the ORETF submission "Evaluation of Transferable Turf Residue Techniques "(MRID# 4497203)" which recommends the California roller as the ORETF technique for conducting TTR studies. Therefore, why were the studies not accepted when the modified California Roller technique and the ORETF Technique are identical ?

Bayer is also concerned about the statement that HED does not considered TTR values less than 1% of the application rate to be acceptable. Granular formulation have consistently been demonstrate to have TTR values less than 1% of the application rate. This statement appears to relate to the relationship between the generic residential SOP transfer coefficients of 14,500 cm^2/hr and 8200 cm^2/hr for children and TTRs less than 1% of the application rate (HED policy 12, revised 22 February 2001). Policy 12 states that the revised transfer coefficients should not be used with TTRs of less than 1% of the application rate. Based on policy 12, transfer coefficients of 43000 cm^2/hr for adults and 8700 cm^2/hr for children are to be used when the TTR values are less than 1%. Therefore, the Oxadiazon TTR studies not considered to be acceptable should be reevaluated and used with higher transfer coefficients if the TTRs are less than 1%.

RESPONSE: HED agrees that the California roller technique is the most efficient of all the measuring techniques to collect TTR data. However, a transfer coefficient (TC) measurement should be taken concurrently with the TTR measurement. In the absence of a concurrent TC measurement, HED's Expo SAC Policy 12 indicates that the default TC values and 5% of application rate for TTR should be used to estimate short-term exposure.

In the submitted Bayer study, the TTR values measured were 0.07% of application rate for granular and 0.15% of application rate for liquid. HED Exposure SAC and the Oxadiazon ORE RED chapter clearly address this policy issue. That is, if either condition applies:

1) TTR collected via California roller technique in absence of concurrent TC values, and/or

2) TTR values< 0.5% of application rate for granular and < 1% for liquid applications

then, HED uses default values as per residential SOP (Policy 12, revised 22 February 2001) for conducting exposure assessment.

The use of low TTRs with the current transfer coefficients may underestimate dermal exposure. HED further reviewed Science Advisory Council Exposure Policy 12 (February 22, 2001) and concluded that transfer coefficients of 43000 cm^2/hr for adults or 8700 cm^2/hr for children have been changed to 14,500 cm^2/hr for adults and 5,200 cm^2/hr for children (1-6 yrs) in the current revised SOP (February 22, 2001). Based on these considerations, the Agency does not change its position on the default values or the TCs used in this risk assessment.

c. Default values

Bayer contends that the golf course TCs developed concurrent TTR monitoring using the modified California method. Therefore, the TTRs obtained from the submitted Ronstar WP study should be used in lieu of the default 5% value.

RESPONSE: The submitted study (MRID# 43517801) measured the exposure associated with Jazzercise on turf. Jazzercise actions are significantly different from golfing actions, therefore, it is not appropriate to use the TTR values obtained from this study as surrogate data. HED used the standard default value from the SOP.

Bayer further contends that the TTR values on p. 35 of the ORE document should be based on the result of the Ronstar WP study and not the default values of 5%. Defaults stated in the residential SOPs are to be used only in the absence of chemical-specific data.

RESPONSE: The tables on pages 37 (Table 8), 38 (Table 9) and 39 (Table 10) of the revised Human Health Risk Assessment use the TTR values from study (MRID# 43517801). The tables also show the risk ***if*** the standard default value is used. HED typically provides a range of risk estimates based on defaults and chemical specific data to SRRD, if required. However, risk managers base their final decision on all of the data shown for these scenarios.

d. Table verification

The Registrant believes that the information on Table 10, p.39 should be verified. Bayer does not understand how the percent values for the hand-to-mouth activities were derived, and why the TTR values are higher for the exposure from irrigated grass than the one for the non-irrigated grass, while the TTR based on study MRID 43517801 indicates the reverse situation. Values presented in Table 10, MRID 43517801 are different from the values presented in the revised Occupational and Residential Exposure Assessment document page 28 provides the following TTR values for non-

irrigated and the irrigated plots: " on day 0, the highest average turf-transferable residues (TTR) for non-irrigated plots was 1.22 μg per cm^2 and 0.694 μg per cm^2 on irrigated plot.".

RESPONSE: The turf-transferable residues (TTR) values indicated on page 28 of the ORE document were obtained from the study MRID 43517801. This study was conducted with 3.0 lb ai/A. In Tables 8, 9 and 10 the TTR values have been adjusted to reflect the label rate of 4.0 lb ai/A. A correction has been made to Table 10 in the revised Human Health Risk Assessment and in the ORE document to present the correct TTR values for irrigated grass versus non-irrigated grass.

HUMAN HEALTH RISK ASSESSMENT

FOR

OXADIAZON

PC Code No. 109001

U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)

Nancy McCarroll, Risk Assessor

OXADIAZON RISK ASSESSMENT

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1.0 EXECUTIVE SUMMARY

The Agency has conducted a human health risk assessment for the active ingredient oxadiazon, [2-tert-butyl-4-(2,4-dichloro-5-isopropoxyphenyl)-*delta 2*- 1,3,4-oxadiazolin-5-one], for the purpose of making a reregistration eligibility decision. Oxadiazon is a selective pre-emergent and early post emergence herbicide registered to control annual grasses and broadleaf weeds. The trade name for oxadiazon in the U.S. is Ronstar®. The Registrant, Bayer Environmental Science is supporting use of oxadiazon on turf (e.g., golf courses, apartment/condo lawns, athletic fields, parks, playgrounds and cemeteries) and ornamentals (Gorrell, 2001). Like other oxadiazoles, it displays light-dependent phytotoxicity through the inhibition of protoporphyrinogen oxidase, an enzyme critical in the biosynthesis of chlorophyl and heme. Accumulation of protoporphyrin IX following exposure to oxadiazon has been demonstrated in plants, yeast and mouse liver mitochondria. Bayer is not supporting any tolerances for oxadizon in the United States (Gorrell, 2001). **There is also no CODEX (Canadian or Mexican tolerances) for oxadiazon (Piper, 2001a). The request for revocation of tolerances for residues of oxadiazon on food and feed has been granted and tolerances will be revoked (Piper, 2001b). Since only the non-food uses of oxadiazon on turf and ornamentals will be retained, it has been determined that a Food Quality Protection Act (FQPA) assessment was not required. Based on the current and anticipated use patterns, dietary risk assessments are also not required.**

Oxadiazon is applied via hand held sprayers, manual spreaders and tractor-drawn equipment. **Aerial application was voluntarily canceled by the Registrant.** This pesticide can be applied at a frequency of 1 to 3 applications per season and at an application rate of 2.0 to 4.0 pounds ai/acre. Use sites include golf courses, roadsides and nurseries. **In addition, oxadiazon may be applied by commercial operators to landscapes (which could include residential landscapes such as apartment/condo lawns, parks, playing fields and cemeteries), and these use patterns indicate a potential non-occupational exposure for adults and children.** Two formulations are available: wettable powder and granular.

Oral toxicity is well characterized for oxadiazon but dermal and inhalation toxicity are not. Accordingly, the short and intermediate-term toxicological endpoints selected for the dermal and inhalation risk assessments were based on an oral endpoint from a rat developmental study. In this study, a **NOAEL[13] of 12 mg/kg/day** was selected based on an increased incidence of fetal loss. A dermal absorption rate of 9% was applied to the dermal risk assessments and a 100% absorption rate was applied to the inhalation risk assessments.

In both subchronic and chronic studies, the major target organ of oxadiazon is the liver. Effects were consistent among the species tested (rat, dog, mouse) and typically included enlarged livers along with increases in serum clinical chemistry parameters associated with hepatotoxicity. The hematopoietic system also appeared to be a target of oxadiazon in all three species, based on mild

[13]No Observable Adverse Effect Level

anemia (reductions in RBC, hematocrit and/or hemoglobin). This is consistent with its ability to inhibit protoporphyrinogen oxidase. In a rat metabolism/pharmacokinetic study, oxadiazon was extensively metabolized, primarily via hydroxylation and glucuronide conjugation. The MARC[14] concluded, however, that the only residue of concern is the parent compound, oxadiazon because major degradates would only be minor components in the enviroment and are not likely to be significantly more toxic than the parent (Piper, 2001b).

The Office of Pesticide Programs (OPP) Carcinogenicity Peer Review Committee (CARC) has classified oxadiazon as **"likely to be carcinogenic to humans"** based on the combined incidence of male mouse liver adenoma and/or carcinoma rates in the ICR-JCL mouse strain. A quantitative risk **(Q_1*) of 7.11 x 10^{-2} $(mg/kg/day)^{-1}$** in human equivalents was used for the human health risk assessments.

Findings from reproduction and developmental toxicity studies indicate that there is no quantitative evidence of increased susceptibility of rats or rabbits following in utero or postnatal exposure to oxadiazon. Similarly, there is no evidence of neurobehavioral alterations, neuropathological effects or neurodevelopmental potential in any of the available toxicity studies.

HED[15] has determined that there are potential exposures to occupational mixers, loaders, applicators, or other occupational handlers during standard use-patterns associated with oxadiazon. Fourteen major exposure scenarios were identified for occupational exposure of handlers. These scenarios include mixing, loading and applying through the use of ground spray, granular and lawn application methods. The exposure scenarios are of short-term (1-7 days) and intermediate-term (1 week to several weeks); use patterns do not indicate any long-term use. The target MOE[16] of 100 for occupational exposure scenarios was selected based on the uncertainty factors of 10x for intraspecies variation and a 10x for interspecies extrapolation. Since the effects from dermal and inhalation exposure are based on the same oral study (i.e., rat developmental study), the doses for these routes and durations were aggregated.

Calculation of **non-cancer occupational risk** based on combined dermal and inhalation exposure indicates that **with the exception of one scenario [i.e., low pressure handwand - wettable powder formulations (with the feasible level of mitigation)], all other potential exposure scenarios provide at least one application rate with total MOEs $\geq$100** at baseline or with PPE[17] or engineering controls. Dermal exposure, rather than inhalation exposure, appears to be the main contributor to the total MOE for the low pressure handwand - wettable powder formulation scenario as well as the majority of occupational exposures.

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[14]Metabolism Assessment Review Committee

[15]Health Effects Division

[16]Margin of Exposure

[17]Personal Protective Equipment

Cancer risks for occupational dermal and inhalation exposures range from 1.65E-2 to 4.66E-7 at baseline, 1.05E-3 to 1.38E-7 with PPE or 4.92E-5 to 1.10E-8 with engineering controls. **Overall, these data suggest that none of the evaluated scenarios have cancer risks that exceed 1.00E-4 (the Agency's level of concern for occupational cancer risk begins at ≤ 1.00E-4 with all attempts to mitigate risks to ≤ 1.00E-6, when possible).**

Postapplication contact of workers with oxadiazon is generally minimal because of the use sites (turf, conifer nurseries, sod farms, landscape-industrial sites or herbaceous ornamental crops early in the season, either pre-plant or before weeds) and the mechanization (machine harvesting and mowing) utilized in cultivating these crops reduces the postapplication contact of workers with oxadiazon. Nevertheless, the Agency has ascertained that there are potential postapplication exposures to individuals re-entering treated areas associated with the following scenarios: mowing roadsides, Bermuda grass right-of-ways, sod farms and golf courses as well as harvesting sod farms. Since oxadiazon is not volatile (has a low vapor pressure of $1.0x10^{-6}$ mm Hg) and is used outdoors, the inhalation component of postapplication exposure is anticipated to be negligible. **Hence, the dermal route is the route of consequence. For short and intermediate-term occupational non-cancer risks, transplanting and/or harvesting weeds either manually or mechanically, had MOEs (30) that failed to meet the target MOE of 100. All other occupational postapplication activities had MOEs of 1000. Cancer risks for occupational postapplication scenarios were estimated not to exceed HED's level of concern (i.e., ≤ 1.00E-4).**

The oxadiazon labels indicate that use of this pesticide is limited to licensed operators and the product is not available to homeowners. **However, there are potential postapplication dermal exposures to adults and toddlers entering oxadiazon-treated lawns and potential postapplication risks to toddlers from incidental ingestion of turfgrass and/or "hand-to-mouth" exposure when entering lawns treated with the granular and wettable powder formulations**. For these assessments, the duration of postapplication dermal exposure is expected to be either short-term or intermediate-term, based on oxadiazon turf residue dissipation data. The short-term and intermediate-term MOEs for dermal exposures were calculated using a NOAEL of 12 mg/kg/day; this value was derived from the same developmental rat study used for the occupational handler noncancer exposures. For the cancer risk estimates, the Q1* of 7.11×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents was used.

Results show that all non-cancer dermal scenarios developed for adults and toddlers had short-term and intermediate-term dermal MOEs greater than 100. The cancer risks for all adult residential dermal postapplication exposures fell between $1.59x\ 10^{-5}$ to 7.51×10^{-7}.

Estimated incidental oral exposure ("hand-to-mouth") for toddlers had an MOE of 100 using the TTR[18] default values from the residential SOP. When the TTR data from the submitted oxadiazon study were used, however, the MOEs were 90 to 240. The former MOE does not exceed the target

[18]Turf Transferable Residue

value of 100; nonetheless, the TTR data from the submitted study were for the wettable powder formulation and the major use of oxadiazon is with the granular formulation. It is probable, therefore, that the risk indicated when the TTR data from the submitted study were applied, is an overestimate and not likely to be a cause for concern. MOEs were not calculated for the incidental ingestion of oxadiazon granules because an acute RfD was not selected for this non-food use pesticide. Additionally, there is no indication from the studies in the guideline database that a single oral exposure to oxadiazon presents a hazard. This statement is also supported by the high rat acute oral LD50 for oxadiazon (>5,000 mg/kg). It is thought, therefore, that the incidental ingestion of granules is not likely to be a cause for concern.

Monitoring data for oxadiazon residues in surface and ground water were not available. Consequently, potential exposures and risks from oxadiazon residues in **unfinished** drinking water were assessed using Tier II PRZM/EXAM (surface waters) and SCI-GROW (ground water) modeling estimates. For risk assessment purposes, surface water EDWCs[19] of oxadiazon were an acute (peak) value of **181 ppb (μg/L)** basing the EDWCs for Oxadiazon on the proposed maximum application rate of 8.0 lbs a.i./A and 3 applications to a golf course (constituting the major use of the pesticide). Ground water EDWCs were average annual value of **100 ppb (μg/L)**. These values generally depict worst-case scenarios, and represent the upper-bound estimates of the concentration that might be found in surface water and ground water due to the use of oxadiazon on turf. These model estimates were compared to DWLOCs[20], the theoretical concentration of pesticide in drinking water that would be an acceptable upper limit in light of the aggregate exposure to the pesticide from other sources. **Results for acute DWLOC calculations show that acute exposure of each population (U.S. population, females 13-50 years, children 1-6 years and infants) to residues of oxadiazon in surface and ground water are of no concern. For chronic DWLOCs, the U.S. population as a whole had a DWLOC value that exceeded the surface and ground water targets. The chronic DWLOC values derived for infants and children exceeded the EDWCs for ground water but not for surface water. Despite the PRZM/EXAM modeling for surface waters, the chronic DWLOCs for infants and children (36 μg/L) are still lower than the refined value (65 μg/L). Hence, the Agency has concerns for children chronically exposed to oxadiazon in drinking water derived from surface waters. In addition, EDWCs for both surface and ground water were higher than the cancer DWLOC; therefore, the cancer risk exceeds HED's level of concern for lifetime exposure to oxadiazon in surface and ground water**. It should be noted, however, that EDWC values derived from the PRZM/EXAM and SCI-GROW models represent the compounding of several worst case scenarios. Similarly, the SCI-GROW model used for the ground water analysis, is based on high concentrations observed in shallow ground water after agricultural treatment of permeable soils. Since this combination of conditions is encountered in only 1% of the agricultural use area in the U.S., it is not likely that oxadiazon would pose a potential cancer concern for exposure to oxadiazon in ground water (Barrett, 1998).

[19]Estimated Drinking Water Concentrations

[20]Drinking Water Levels of Concern

The RARC[21] recommended that an aggregate risk assessment not be conducted on oxadiazon because the DWLOC values are based on conservative default values since no monitoring data were available on oxadiazon and the refined model for turf analysis is not completed at this time. In addition, data used to develop residential exposure estimates (dermal exposure values) were also conservative because the highest mean postapplication TTR residue value from the submitted study along with the data from the wettable powder formulation were used . Thus, any aggregation of a conservative water number with a conservative residential exposure estimate would result in an even more conservative expression of aggregate risk. The RARC also noted that guidance from management on this issue is forthcoming.

Oxadiazon **has not** been reported to cause life-threatening illness or death in humans. Most of the cases appear to be related to irritation to the skin, eyes and mucous membranes. Some cases may be related to an allergic reaction. On the list of the top 200 chemicals for which NPTN[22] received calls from 1984-1991 inclusively, oxadiazon was ranked 192nd with 12 incidents in humans reported and 5 incidents in animals (mostly pets).

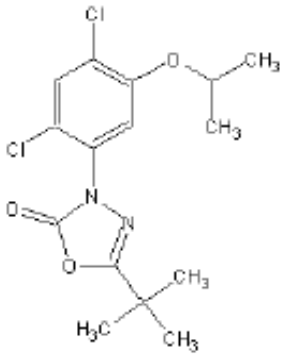
In summary, the potential risks from occupational exposure to oxadiazon are generally below HED's level of concern. **However, even with the feasible level of mitigation, there is one occupational exposure scenario (i.e., low pressure handwand-wettable powder formulations) and there are postapplication occupational exposures associated with transplanting and/or harvesting weeds manually or mechanically that are of concern.** HED also had concerns for chronic and lifetime exposure to oxadiazon in drinking water derived from surface and/or ground water.

[21]Risk Assessment Committee

[22]National Pesticide Telecommunication Network

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Oxadiazon [2-tert-butyl-4-(2,4-dichloro-5-isopropoxyphenyl)-*delta*-2-1,3,4-oxadiazolin-5-one] is a preemergence, early postemergence herbicide registered to control annual grasses and broadleaf weeds.



Oxadiazon

Empirical formula: C15H18Cl 2N2O 3
Molecular weight: 345.2
CAS Registry No.: 19666-30-9
PC Code: 109001

Oxadiazon is an odorless white crystalline powder with a melting point of 90°C, a density of 1.3 gm/mL and it has a low solubility in water (0.0007 g/L at 20°C). It is stable at normal and elevated temperatures (at 55°C), stable in the presence of metals (aluminum, iron and tin) and metal ions (ferric chloride), and has a low vapor pressure ($1.0x10^{-6}$ mm Hg). A single manufacturing use product (MP) registered under the PC Code 109001 was identified as Bayer Environmental Science USA LP 94% technical (T); only this Bayer 94% T is subject to the RED (Dockter, 2001; Piper, 2001). The Registrant lists oxadiazon as not leaching and persistent in soil (Dockter, 2001). Both the Product Chemistry and the Residue Chemistry databases for oxadiazon are complete.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Oxadiazon is a selective pre-emergent herbicide of the oxadiazole class. Like other oxadiazoles, it displays light-dependent phytotoxicity through the inhibition of protoporphyrinogen oxidase. Accumulation of protoporphyrin IX following exposure to oxadiazon has been demonstrated in plants, yeast and mouse liver mitochondria.

Details of the hazard assessment of oxadiazon can be found in the HED's Toxicology Disciplinary Chapter (Hansen and McCarroll, 2001); major features of the toxicology profile are presented below. In acute studies, oxadiazon is only slightly toxic (Toxicity Categories III or IV) with an oral LD_{50} >5000 mg/kg, a dermal LD_{50} >2000 mg/kg and an inhalation LC_{50} > 1.94 mg/L. Oxadiazon is mildly irritating to ocular tissue and negligibly irritating to the skin (both Toxicity Category III) and is not a dermal sensitizer (Table 1).

Table 1. Acute Toxicity Data on Oxadiazon

Guideline No./ Study Type	MRID No.	**Results**	**Toxicity Category**
870.1100 Acute oral toxicity (rat)	41866501 (97.5% a.i.)	LD_{50} >5000 mg/kg ♂, ♀ combined	IV
870.1200 Acute dermal toxicity (rabbit)	41866502 (97.5% a.i.)	LD_{50} >2000 mg/kg, ♂, ♀ combined	III
870.1300 Acute inhalation toxicity (rat)	41866503 (93.7% a.i.)	LC_{50} >1.94 mg/L ♂, ♀ combined	III
870.2400 Acute eye irritation (rabbit)	41866504 (97.5% a.i.)	Mild irritant to ocular tissues	III
870.2500 Acute dermal irritation (rabbit)	41866505 (97.5% a.i.)	Negligibly irritating to skin	III
870.2600 Skin sensitization (guinea pig)	41230401 (93.7% a.i.)	Not a dermal sensitizer (Buehler test)	--
870.6200a Acute neurotoxicity screening battery (rat)	ND	--	--

ND No data - not required for oxadiazon.

The major target organ of oxadiazon is the liver. Effects were consistent among the species tested (rat, dog, mouse) in both subchronic and chronic studies and typically included enlarged livers along with increases in serum clinical chemistry parameters associated with hepatotoxicity such as alkaline phosphatase and serum aspartate or alanine aminotransferase. Findings in rats and mice

included fatty changes, pigmented Kupffer cells and bile canaliculi and bile duct proliferation, periacinar swelling and pallor, increased acidophilic cells, hyperplasia and hepatocellular necrosis. No treatment-related microscopic lesions were observed in the subchronic dog study and findings in the chronic study were only observed at the highest dose tested (200 mg/kg/day), where only two animals/sex were assigned and one female was sacrificed in moribund condition. These findings included increased liver weight and hepatocellular histopathology (centriacinar vacuolation, periacinar apoptosis and inflammation). The hematopoietic system also appeared to be a target of oxadiazon in all three species, based on mild anemia [reductions in red blood cells (RBC), hematocrit and/or hemoglobin]. This is consistent with its its ability to inhibit protopotphyrinogen oxidase, an enzyme involved in the synthesis of both heme and chlorophyll. In addition to effects on the liver, increased pigmentation in the kidney was observed in rats, along with increased blood urea nitrogen (BUN) and kidney weights. Although a dose-dependent increase in thyroid weight was observed in the dog subchronic oral toxicity study and at the highest dose tested of the chronic dog studies, treatment-related changes in thyroid weights or gross/microscopic observations were not observed in other studies (thyroid hormones were not evaluated). In general, males appeared to be slightly more sensitive to oxadiazon than females.

Oxadiazon is not readily absorbed by the skin. In a rat dermal absorption study, up to $\approx$9% of the applied dose of technical oxadiazon was absorbed after 10 hours of exposure, this includes 2.65% absorbed and 6.07% which could be potentially absorbed. The 21-day rabbit dermal toxicity study supports low dermal absorption: no toxicity was observed at the limit dose of 1000 mg/kg/day.

Following long-term dietary administration, oxadiazon caused an increased incidence of hepatocellular adenoma and carcinoma in rats and mice. Consistent findings were reported in a total of four acceptable studies in two species (2 mouse and 2 rat studies). A third mouse study was unacceptable, although increased hepatocellular tumors were also observed in mice of both sexes. In CD-1 mice, statistically significant increases of hepatocellular adenoma and combined adenoma/adenocarcinoma were observed at all dose levels tested ($\geq$100 ppm) in both males and females. The incidence of hepatocellular carcinoma was increased at all doses in males but only at the two highest doses in females. The highest dose tested exceeded the maximum tolerated dose (MTD) for males, based on excessive mortality. In ICR-JCL mice, adenomas, carcinomas and combined adenomas/carcinomas were increased in males at the two highest doses but only at the highest dose in females. In SPF Wistar rats, the incidence of hepatocellular adenomas, carcinomas and combined adenomas/carcinomas was increased in males only. A second study in F344 rats showed a treatment-related increase in the incidence of hepatocellular carcinoma and combined adenoma/carcinoma only in males. A classification of "likely to be carcinogenic to humans" was assigned by the CARC[23] using the EPA Draft Guidelines for Carcinogen Risk Assessment of July 1999 (Diwan, 2001). A quantitative risk (Q1*) of 7.11×10^{-2} $(mg/kg/day)^{-1}$ was calculated as the most potent unit risk, based on the incidence of male mouse liver adenoma and/or carcinoma combined tumor rates in the ICR-JCL mouse (Brunsman, 2001).

[23]Cancer Assessment Review Committee

In a special submitted mechanistic study in rats and a published study in rats, mice and dogs, oxadiazon induced peroxisomal proliferation (based on liver enlargement, peroxisomal enzyme induction and electron microscopy) after a 14-day dietary administration. Some peroxisomal proliferator compounds are known to be liver carcinogens, but the HED MTARC[24] determined that there are insufficient data available to support this as a mechanism of carcinogenicity for oxadiazon due to insufficient data showing hepatocellular proliferation, lack of concordance between the enzyme induction dose-response and tumor formation and an unexplained decrease in catalase, which is normally significantly increased by peroxisomal proliferator compounds (McCarroll, 2001a).

Oxadiazon did not show mutagenic potential in any in vitro assays with bacteria *(S. typhimurium* and *E. coli)* or mammalian cells (TK +/-mouse lymphoma cells), did not show clastogenic potential in the *in vitro* Chinese hamster ovary cell chromosomal aberration assays and did not induce unscheduled DNA synthesis in cultured primary rat hepatocytes. However, a dose-related increase in transformation frequencies was observed in an in vitro Syrian hamster kidney BHK21 C13/HRC1 cell transformation assay.

Significant fetal toxicity (fetal loss due to resorptions and post-implantation loss, decreased fetal weight, skeletal variations) was observed in developmental toxicity studies in both rats and rabbits. These fetal effects occurred at the same dose levels at which slight maternal toxicity (decreased weight gain/weight loss) were observed. Offspring survival effects were also observed in the rat two-generation reproduction study. No toxicity was reported at the lowest dose tested; however, in the range-finding phase of the reproduction study at higher dose levels, fetal and neonatal survival were also sharply reduced. The decreased neonatal survival was due at least in part to effects on lactation, based on findings of inactive mammary glands in the dams at necropsy. It is likely that neonatal loss may have resulted from starvation and would, therefore, be an effect of direct maternal toxicity. Inactivity of the mammary tissue as a possible effect of endocrine disruption was considered by the HIARC[25] but was not found to be likely since there was no evidence from any other study in the database suggesting endocrine disruption (McCarroll, 2001 b). No fetal malformations were observed in the rat or rabbit developmental toxicity studies; however, some skeletal variations (delayed ossification, asymmetric pelvis) were reported. The above findings indicate that there is no quantitative evidence of increased susceptibility of rats or rabbits following *in utero* or postnatal exposure to oxadiazon.

Neurotoxicity studies are not required for oxadiazon because no clinical signs of toxicity suggestive of neurobehavioral alterations nor evidence of neuropathological effects were observed in any of the available toxicity studies. There was no evidence for neurodevelopmental potential of oxadiazon in the rat and rabbit developmental toxicity studies, nor in the rat two-generation reproductive toxicity study.

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[24]Mechanism of Toxicity Assessment Review Committee

[25]Hazard Identification Assessment Review Committee

In a rat metabolism/pharmacokinetic study, oxadiazon was extensively metabolized, primarily via hydroxylation and glucuronide conjugation. Eighteen (18) metabolites were identified in the urine and feces, of which 4 urinary and 5 fecal metabolites were present at levels greater than 1% of the dose. After 7 days, ≥83% of the administered dose was excreted in the urine and feces (total recovery ≥94%) for all dose groups. Females excreted more radioactivity in the urine than males. The excretion of radioactivity into the urine and the feces was sex dependent and the tissue residues were very low in all tissues except liver and fat. Low doses (5 mg/kg, single or multiple) of oxadiazon were completely absorbed, metabolized and excreted in the urine and feces and virtually no free oxadiazon was found in the urine. At this dose, the rates and routes of excretion of radioactivity were similar. At high dose (500 mg/kg), the rate of excretion was affected but the route was not. Intact oxadiazon was present in feces only and was dose-related: at the high dose, more than 53% of the administered radioactivity was intact oxadiazon in the feces; at 5 mg/kg, not more than 4.8% of the dose was intact oxadiazon in the feces. Based on the available data, the MARC concluded that the only residue of concern is the parent compound, oxadiazon because major degradates would only be minor components in the enviroment and are not likely to be significantly more toxic than the parent (Piper 2001b). Subchronic, chronic and other types of toxicity studies are summarized in Table 2.

The only data gap that has been identified at this time is a 28-day inhalation study (OPPTS No. 870.3465). This study is not a guideline requirement for oxadiazon, but has been requested by the Agency because some currently registered products of oxadiazon include spray formulations (McCarroll, 2001 b) which could result in exposure via the inhalation route.

3.2 FQPA Considerations

From the available data, it was concluded that there is no quantitative evidence of increased susceptibility of rats or rabbits following *in utero* or postnatal exposure to oxadiazon. **However, it has been determined that an FQPA assessment is not required because oxadiazon has no food or feed uses; the request for revocation of tolerances for residues of oxadiazon on food and feed has been granted and tolerances will be revoked (Piper, 2001b).**

Table.2 Subchronic, Chronic and Other Toxicity Tables

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
SUBCHRONIC TOXICITY STUDIES		
870.3100 90-Day oral toxicity (CD rat)	00111804 (1970) Acceptable/guideline 0, 25, 100 or 1000 mg/kg/d (diet)	NOAEL = 25 mg/kg/day LOAEL = 100 mg/kg/day based on decreased body weight, increased liver weight, hematological changes and clinical chemistry and pathological changes associated with liver damage.
870.3150 90-Day oral toxicity in (Beagle dog)	00111805 (1970) Acceptable/guideline 0, 25, 100 or 1000 mg/kg/d (capsule)	NOAEL <25 mg/kg/day LOAEL ≤25 mg/kg/day based on increased thyroid weights in males.
870.3200 21-Day dermal toxicity (NZW rabbit)	41863602 (1991) Acceptable/guideline 0, 100, 500 or 1000 mg/kg/day	NOAEL ≥ 1000 mg/kg/day. LOAEL > 1000 mg/kg/day.
DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES		
870.3700a Prenatal developmental (SD rat)	40470202 (1987) Acceptable/guideline 0, 3, 12 or 40 mg/kg/day (gavage)	**Maternal** NOAEL = 12 mg/kg/day. LOAEL = 40 mg/kg/day based on decreased body weight/weight gain. **Developmental** NOAEL = 12 mg/kg/day LOAEL = 40 mg/kg/day based on increased fetal resorptions/implantation loss, decreased pup weight and increased incidence of incomplete ossification.
870.3700b Prenatal developmental (NZW rabbit)	40470201 (1987) Acceptable/guideline 0, 20, 60 or 180 mg/kg/day (gavage)	**Materna**l NOAEL = 20 mg/kg/day LOAEL = 60 mg/kg/day based on transient weight loss during the first week of treatment. **Developmenta**l NOAEL = 60 mg/kg/day LOAEL = 180 mg/kg/day based on increased postimplantation loss and late resorptions, decreased fetal weight and increased bilateral hind-limb flexure.
870.3800 Reproduction and fertility effects (CD rat)	41239801 (1988) Acceptable/guideline 0, 20, 60 or 200 ppm (M/F 0, 1.5/1.84, 4.65/5.63 or 15.50/18.20 mg/kg/day, premating)	**Parental/Systemic** NOAEL ≥ 15.5 mg/kg/day LOAEL >15.5 mg/kg/day (decreased gestational weight gain in RF study at 38 mg/kg/day). **Reproductive** NOAEL ≥ 15.5 mg/kg/day LOAEL > 15.5 mg/kg/day (inactive mammary tissue, fetal/neonatal mortality in the RF study at 38 mg/kg/day). **Offspring** NOAEL ≥ 15.5 mg/kg/day LOAEL > 15.5 mg/kg/day (fetal/neonatal mortality in the RF study at 38 mg/kg/day).

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
CHRONIC TOXICITY AND CARCINOGENICITY STUDIES		
870.4100a Chronic toxicity (rat)	See 870.4300, Combined chronic toxicity/carcinogenicity	
870.4100b Chronic toxicity (Beagle dog)	41326401(1989) Acceptable/guideline 0, 5, 20 or 60 mg/kg/day (capsule)	NOAEL = 5 mg/kg/day LOAEL = 20 mg/kg/day based on increased absolute and relative female liver weight accompanied by similar changes in liver weight for both sexes at 60 mg/kg/day.
870.4200 Carcinogenicity (CD-1 mouse)	00044322 (1980) Unacceptable/guideline 0, 300, 1000 or 2000 ppm (M/F 0, 48/62, 153/201 or 319/417 mg/kg/day), in diet	NOAEL <48 mg/kg/day LOAEL ≤48 mg/kg/day based on increased liver weight, serum enzymes related to liver damage and microscopic pathology in the liver of both sexes. **Evidence of carcinogenicity**- increased incidence of hepatocellular carcinoma, both sexes at ≥48/62 mg/kg/day.
870.4200 Carcinogenicity (CD-1 mouse)	00115733 (1982) Acceptable/guideline 0, 100, 300, 1000 or 2000 ppm (M/F 0, 12/14, 37/44, 122/143 or 254/296 mg/kg/day), in diet	NOAEL ≤12 mg/kg/day LOAEL < 12 mg/kg/day based on clinical signs, increased liver weights in males and increased microscopic pathology in the liver of both sexes. **Evidence of carcinogenicity** - increased incidence of hepatocellular neoplasms (adenoma, combined adenoma/carcinoma) in both sexes at all doses tested (carcinoma alone increased in all male groups and at ≥143 mg/kg/day in females).
870.4200 Carcinogenicity (ICR-JCL mouse)	40993301 (1987) Acceptable/guideline 0, 3, 10, 100 or 1000 ppm (M/F 0, 0.315/0.278, 1.09/0.92, 10.6/9.3 or 113/99 mg/kg/day), in diet	NOAEL = 1.09 mg/kg/day LOAEL = 10.6 mg/kg/day based on anemia and microscopic lesions in the liver and kidneys (all in males). **Evidence of carcinogenicity** - increased incidence of hepatocellular neoplasms (adenomas, carcinomas and combined adenomas/carcinomas in males at ≥10.6 mg/kg/day and in females at 99 mg/kg/day).
870.4300 Combined chronic toxicity/carcinogenicity (F344 rat)	00149003, 00157780 (1982, 1986) Acceptable/guideline 0, 10, 100, 1000 or 3000 ppm (M/F 0, 0.5/0.6, 5.9/4.8, 50.9/60.9 or 163.1/192.7 mg/kg/day, in diet	NOAEL = 0.5 mg/kg/day LOAEL = 4.8 mg/kg/day based on increased liver weights in both sexes and increased total serum protein in females. **Evidence of carcinogenicity** - increased incidence of hepatocellular neoplasms in males (adenomas and combined adenomas/carcinomas in males at ≥50.9 mg/kg/day).

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300 Combined chronic toxicity/carcinogenicity (Wistar rat)	40993401 (1987) Acceptable/guideline 0, 3, 10, 100 or 1000 ppm (M/F 0, 0.106/0.131, 0.36/0.44, 3.5/4.2 or 39/44 mg/kg/day)	NOAEL = 0.36 mg/kg/day LOAEL = 3.5 mg/kg/day based on increased incidence of hepatocellular centrilobular swelling in males. **Evidence of carcinogenicity**-increased incidence of hepatocellular neoplasms in males (adenomas and combined adenomas/carcinomas at ≥4.2 mg/kg/day and carcinomas at 39 mg/kg/day).
MUTAGENICITY AND CELL TRANSFORMATION STUDIES		
870.5100 Gene Mutation Bacterial reverse gene mutation assay and 870.5500 Bacterial DNA Repair Assay	00069893 (1976) Acceptable/guideline *S. typhimurium* and *E. coli* 100-2500 and 10-1000 μg/plate w/o S9 and 10-1000 μg/plate w/S9. *B. subtilis* 20-2000 μg/plate w/o S9.	Negative in *S. typhimurium* strains TA1535, TA1437, TA1538, TA98 and TA100; *E. coli* strain WP2 *hcr*$^-$ and *B. subtilis* strains H17 and M45 (cytotoxicity not observed).
870.5100 Gene Mutation Bacterial reverse gene mutation assay	41871701 (1991) Acceptable/guideline 50-5000 μg/plate w/o or w/S9.	Negative in *S. typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 (cytotoxicity observed at ≥3330 μg/plate w/o S9 but not w/S9). Insoluble at ≥500 μg/plate.
870.5300 Gene Mutation *In vitro* mammalian cell forward gene mutation assay	00115726 (1982) Acceptable/guideline 15.6-1000 μg/mL (Trial 1), 50-1000 μg/mL (Trial 2), both w/o S9; 3.91-62.5 (Trial 1), 20-100 (Trial 2) and 100-200 μg/mL (Trial 3), all w/S9.	Negative in L5178Y TK$^+$ mouse lymphoma cells (cytotoxicity observed at 1000 μg/mL w/o S9 and ≥200 μg/mL w/S9). Insoluble at ≥62.5 μg/mL.
870.5300 Gene Mutation *In vitro* mammalian cell forward gene mutation assay	00115729 (1982) Acceptable/guideline 31.3-1000 μg/mL w/o S9 and 15.6-250 μg/mL w/S9	Negative in L5178Y TK$^+$ mouse lymphoma cells (cytotoxicity observed at 1000 μg/mL w/o S9 and 250 μg/mL w/S9). Insoluble at 250 μg/mL.
870.5375 Cytogenetics *In vitro* mammalian cell chromosomal aberration assay	00115728 (1982) Acceptable/guideline 2-2000 μg/mL w/o S9; 0.667-2000 μg/mL (Trial 1) and 200-600 μg/mL (Trial 2), both w/S9.	Negative in Chinese hamster ovary (CHO) cells (cytotoxicity observed at 200 μg/mL w/o S9 and 500 μg/mL w/S9). Insoluble at 667 μg/mL w/o S9 and 200 μg/mL w/S9.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.5375 Cytogenetics *In vitro* mammalian cell chromosomal aberration assay	00115730 (1982) Acceptable/guideline 0.416-125 μg/mL (Trial 1) and 12.5-75 μg/mL (Trial 2), both w/o S9; 1.25-125 μg/mL w/S9 (trial 2).	Negative in Chinese hamster ovary (CHO) cells (cytotoxicity at 75 μg/mL w/o S9 and 41.6 μg/mL w/S9). Insoluble at 416 μg/mL.
870.5395 Cytogenetics Mammalian erythrocyte micronucleus test	0073288 (1980) Unacceptable/guideline (not upgradable) 0, 500, 1000 or 2000 mg/kg 100% oxadiazon	Negative up to limit dose of 2000 mg/kg, but early sampling time (6 hr post-dosing) may have missed peak time of mutagenic effect. No signs of toxicity were observed.
870.5395 Cytogenetics Mammalian erythrocyte micronucleus test	0073289 (1980) Unacceptable/guideline (not upgradable) 0, 500, 1000 or 2000 mg/kg	Negative up to limit dose of 2000 mg/kg , but early sampling time (6 hr post-dosing) may have missed peak time of mutagenic effect. No signs of toxicity were observed.
870.5395 Cytogenetics Mammalian erythrocyte micronucleus test	00732890 (1980) Unacceptable/guideline (not upgradable) 0, 500, 1000 or 2000 mg/kg 24865 RP (99%), an oxadiazon impurity	Negative up to limit dose of 2000 mg/kg, but early sampling time (6 hr post-dosing) may have missed peak time of mutagenic effect. Clinical signs of toxicity observed at $\geq$1000 mg/kg including 2 deaths at 2000 mg/kg.
870.5550 Other Effects Unscheduled DNA synthesis assay	00115723 (1982) Acceptable/guideline 1.0 to 1000 μg/mL	Negative in primary rat hepatocytes after 18 hrs (cytotoxicity observed at 100-500 μg/mL).
870.5550 Other Effects Unscheduled DNA synthesis assay	00115727 (1982) Acceptable/guideline 0.5 to 50 μg/mL	Negative in primary rat hepatocytes after 18 hrs (cytotoxicity observed at 50 μg/mL).

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
Nonguideline Other Effects *In vitro* cell transformation	00115703 (1982) Acceptable/nonguideline 12.5-200 μg/mL w/ and w/o S9 for technical oxadiazon; 25-400 μg/mL for recrystallized oxadiazon (100%) w/S9 or w/o S9.	**Positive**, dose-related induction of cell transformation above background levels observed w/S9 and w/o S9 activation in Syrian hamster kidney cells (BHK21 C13/HRC1 cells) for both technical and recrystallized oxadiazon.
METABOLISM, DERMAL PENETRATION AND SPECIAL MECHANISTIC STUDIES		
870.7485 Metabolism and pharmacokinetics (Crl:CD(SD)BR rat)	42324701, 42663601 (1992, 1993) Acceptable/guideline 5 mg/kg ^{14}C-oxadiazon (single dose), 5 mg/kg (14-day dose of oxadiazon + 1 dose of ^{14}C-oxadiazon, day 15) or 500 mg/kg ^{14}C-oxadiazon (gavage)	At 5 mg/kg, oxadiazon is completely absorbed, metabolized and excreted in urine and feces (no parent compound in urine; <5% in feces). At 500 mg/kg, 53% of administered dose was excreted in feces as parent compound. For both groups, $\geq$83% of administered dose was excreted in urine and feces (total recovery $\geq$94%) by 7 days' post-dosing. Females tended to excrete more radioactivity in urine than males. Oxadiazon was metabolized primarily by hydroxylation and glucuronide conjugation, but benzene and pyrozolidine rings were not metabolized. A total of 18 metabolites were identified in urine and feces (4 urinary, 5 fecal metabolites present at >1% of administered dose).
870.7600 Dermal penetration (SD rat)	44588101(1996) Acceptable/guideline 5.45, 39.2 or 523 μg/cm^2 (exposure times of 0.5, 1, 2, 4, 10 or 24 hrs)	Total absorption $\approx$9% of administered dose (96% a.i.) following 10 hr exposure (2.65% absorbed and 6.05% potentially absorbed by skin). Absorption but not dermal uptake saturated at 39.2 and 523 μg/cm^2.
Special studies (nonguideline) - Peroxisomal proliferation (SD rat)	42310001 (1991) Acceptable/nonguideline 0, 20, 200 or 500 mg/kg/day in diet for 14 days	NOAEL <20 mg/kg/day. LOAEL = 20 mg/kg/day, based on increased peroxisomal enzyme (palmitoyl CoA and acetylcarnitine transferase) activities. At 200 mg/kg/day, liver enlargement and at 500 mg/kg/day, ultrastructural changes (peroxisomal proliferation and microsomal alterations) were also observed. However, catalase was decreased by treatment.

NOAEL No Observable Adverse Effect Level

LOAEL Lowest Observable Adverse Effect Level

3.3 Dose Response Assessment

On December 7, 2000, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for oxadiazon with regard to the toxicological endpoint selection for use as appropriate in occupational/residential

exposure risk assessments. Based on these deliberations, the HIARC concluded that neither an acute nor a chronic reference dose was required because there are no food or feed or anticipated food or feed uses for oxadiazon. The HIARC report, nevertheless, indicated that there are toxicological endpoints of concern for oxadiazon. A short-term oral endpoint was selected for incidental oral exposure in children, using a No Observed Adverse Effect Level (NOAEL) of 12 mg/kg/day based on a statistically significant decrease in maternal body weight gains at 40 mg/kg/day (LOAEL) in a developmental study in rats (McCarroll, 2001 b).

For short-term and intermediate dermal exposure, an oral endpoint was selected using a NOAEL of 12 mg/kg/day based on a statistically significant decrease in maternal body weight gains at 40 mg/kg/day (LOAEL) in a developmental study in rats. For the long-term dermal exposure, an oral endpoint was also selected using a NOAEL of 0.36 mg/kg/day, based on an increased incidence of hepatocellular centrilobular swelling in males at 3.5 mg/kg/day (LOAEL) in a combined chronic/oncogenicity feeding study in rats. The HIARC recommended that a dermal absorption factor of 9% (rounded up from 8.7%) be used in the calculations, based on a dermal penetration study.

Due to a lack of inhalation studies, the HIARC selected an endpoint from oral studies for inhalation risk assessments. For short and intermediate-term inhalation exposure, the same oral study was chosen as for dermal exposure of this duration, with a NOAEL of 12 mg/kg/day. The same chronic/oncogenicity feeding study in rats chosen for dermal exposure of this duration was selected for the long-term inhalation exposure, with a NOAEL of 0.036 mg/kg/day. An absorption factor of 100% was applied for inhalation exposures. The **target MOE of 100** for occupational and residential exposure scenarios was selected based upon 10x for intraspecies variation and 10x for interspecies extrapolation. Because the effects from dermal and inhalation exposure are the same, the doses for these routes and duration were combined. Dermal and incidental oral exposures for toddlers were also combined to reflect a total exposure burden.

Since 1987, the Agency's decision on the carcinogenic potential of oxadiazon has been in concurrence with the Scientific Advisory Panel's (SAP) classification of oxadiazon as a **Group C carcinogen and the Q_1* has been set at 1.4 x 10^{-1}(mg/kg/day)$^{-1}$ in human equivalents.** Since that time, new chronic/carcinogenicity data have been submitted and reviewed by the CARC. Based on this revisit, CARC has reclassified oxadiazon as a **"Likely To Be Carcinogenic To Humans"** (Diwan, 2001). For the purpose of the lifetime cancer risk assessment by the Agency, the most potent unit risk, Q_1^*, is that for male mouse liver adenoma and/or carcinoma combined tumor rates at **7.11 x 10^{-2}** (mg/kg/day)$^{-1}$ in human equivalents. All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Brunsman, 2001). The endpoints that were selected for this risk assessment are summarized in Table 3.

Table 3: Endpoints Selected by HIARC for Assessing Occupational and Residential Risks for Oxadiazon			
EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Incidental Oral, Short-Term	NOAEL= 12 Maternal effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL).	Developmental Toxicity -Rat MRID No. 40470202
Incidental Oral, Intermediate-Term	NOAEL= 12 Maternal effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL).	Developmental Toxicity -Rat MRID No. 40470202
Dermal, Short-Term	NOAEL= 12 Maternal effects/ Developmental effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL) / Increased fetal resorptions/postimplantation loss, increased incidence of incomplete ossification at 40 mg/kg/day (LOAEL). **For this risk assessment, the dermal absorption rate of 9% is applied.**	Developmental Toxicity -Rat MRID No. 40470202
Dermal, Intermediate-Term	NOAEL= 12 Maternal effects/ Developmental effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL) / Increased fetal resorptions/postimplantation loss, increased incidence of incomplete ossification at 40 mg/kg/day (LOAEL). **For this risk assessment, the dermal absorption rate of 9% is applied**.	Developmental Toxicity - Rat MRID No. 40470202
Dermal, Long-Term	NOAEL=0.36	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL) / Increased centrilobular swelling in male livers at 3.5 mg/kg/day (LOAEL). **For this risk assessment**, **the dermal absorption rate of 9% is applied.**	Combined Chronic Feeding/ Oncogenicity - Rat MRID Nos. 40993401, 00149003/00157780
Inhalation, Short-Term	NOAEL= 12 Maternal effects/ Developmental effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL) / Increased fetal resorptions/postimplantation loss, increased incidence of incomplete ossification at 40 mg/kg/day (LOAEL). **For this risk assessment, route-to-route extrapolation and a 100% absorption rate are applied**	Developmental Toxicity - Rat MRID No. 40470202
Inhalation, Intermediate-Term	NOAEL= 12 Maternal effects/ Developmental effects	Reduced body weight/body weight gain at 40 mg/kg/day (LOAEL) / Increased fetal resorptions/postimplantation loss, increased incidence of incomplete ossification at 40 mg/kg/day (LOAEL). **For this risk assessment, route-to-route extrapolation and a 100% absorption rate are applied.**	Developmental Toxicity - Rat MRID No. 40470202
Inhalation, Long-Term	NOAEL= 0.36	Increased centrilobular swelling in male livers at 3.5 mg/kg/day (LOAEL). **Route-to-route extrapolation and a 100% absorption rate aplied.**	Combined Chronic Feeding/ Oncogenicity - Rat MRID Nos. 40993401, 00149003/00157780
Cancer	Q_1* of 7.11 x 10^{-2} $(mg/kg/day)^{-1}$	Significant increase (pair-wise and trend, $p<0.01$) in liver adenomas and adenomas and/or carcinomas combined in males at $\geq$ 9.3 mg/kg/day).	Combined Chronic Feeding/ Carcinogenicity - Mouse MRID Nos. 40993301

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

Oxadiazon is applied as a pre-plant or pre-emergent herbicide on non-food/outdoor crops. The Registrant, Bayer Environmental Science is supporting use of oxadiazon on turf (*e.g.*, golf courses, apartment/condo lawns, athletic fields, parks, playgrounds and cemeteries) and ornamentals (Gorrell, 2001). Bayer is not supporting any tolerances for oxadiazon in the United States (Gorrell, 2001)**. There is also no CODEX (Canadian or Mexican tolerances) for oxadiazon (Piper, 2001a). The request for revocation of tolerances for residues of oxadiazon on food and feed has been granted and tolerances will be revoked (Piper, 2001b).** Occupational applications (*i.e.*, to turf and ornamentals) are made to established areas such as lawns or golf course greens prior to the emergence of the target plant species. The oxadiazon labels indicate that use of this pesticide is limited to licenced operators and the product is not available to homeowners. Residential/ non-occupational applications by commercial operators are made to residential lawns, parks, cemeteries, schools, athletic fields and golf courses. The frequency of application ranges from 1 to 3 applications per season. Oxadiazon can be applied at a minimum application rate of 2.0 pounds of active ingredient (ai) per acre up to a maximum application rate of 4.0 pounds ai/acre to turf and ornamentals. Oxadiazon use sites are classified as non-food sites (*i.e.*, primarily golf course greens), residential outdoor use, roadside and nurseries. The granular formulations account for the majority of oxadiazon that is used on turf.

Occupational-use sites include:

Oxadiazon is registered for occupational-use only on conifer nurseries, landscape - industrial sites, ornamental, roadside landscape planting, woody ornamental shrubs, vines and trees, herbaceous ornamental, and turf grass for lawns, fairways, and sod production.

Residential/Non-occupational-use sites include:

Oxadiazon is registered for commercial use on lawns and turf grown in parks, playgrounds, athletic fields, cemeteries, schools and other residential (*i.e.*, residential buildings) areas. It is also used on sod farms and golf courses.

Methods and types of equipment used:

Chemigation, groundboom, rights-of-way sprayer, handgun sprayer, tractor drawn spreader, backpack sprayer, low pressure handwand, high pressure handwand, lawn handgun, belly grinder and push type spreader are examples of the application equipment associated with the use patterns for oxadiazon. **(Aerial application was voluntarily canceled by the registrant).**

4.2 Dietary Exposure

4.2.1 Food Exposure

There are no food or feed or anticipated food or feed uses for oxadiazon. The Registrant is not supporting any tolerances for oxadiazon in the United States (Gorrell, 2001). There is also no CODEX (Canadian or Mexican tolerances)for oxadiazon (Piper, 2001a). The request for revocation of tolerances for residues of oxadiazon on food and feed has been granted and tolerances will be revoked (Piper, 2001a). Consequently, dietary exposure is not a concern for this product.

4.2.2 Water Exposure

The Enviromental Fate and Effects Division (EFED) has provided a surface and groundwater analysis for oxadiazon (Melendez, 2001). The MARC concluded that the only residue of concern is the parent compound, oxadiazon because major degradates would only be minor components in the environment and are not likely to be significantly more toxic than the parent (Piper, 2001b). Thus, they are not likely to be a concern in surface or ground water. Based on environmental fate characteristics, potential exposures and risks from oxadiazon residues in **unfinished** drinking water were assessed using Tier II PRZM/EXAM (surface waters) and SCIGROW (ground water) modeling estimates. For risk assessment purposes, surface water EDWCs[26] of oxadiazon were an acute (peak) value of **181 ppb (μg/L)** using PRZM/EXAMS modeling and basing the EDWCs for Oxadiazon on the proposed maximum application rate of 8.0 lbs a.i./A and 3 applications to a golf course (constituting the major use of the pesticide). The EDWCs for groundwater was an average annual value of **100 ppb (μg/L)**. These values generally depict worse-case scenarios, and represent the upper-bound estimates of the concentration that might be found in surface and ground water due to the use of oxadiazon on turf. In the absence of oxadiazon monitoring data, unique turf characteristics (i.e., turf offers a vegetation interception layer that prevents rapid deposition of pesticides onto the surface of soil and promotes runoff) have been considered in the rationale for developing EDWCs.

4.2.2.1 Surface Water

For drinking water originating in surface water bodies, **an acute concentration of 181 μg/L was used to evaluate the risk to human health.** This amount represents the high-end value that might be found in a small drinking water reservoir. **A chronic value of 100.0 μg/L was used to evaluate the chronic and cancer risk to human health.**

4.2.2.2 Ground Water

For drinking water originating in ground water, the SCI-GROW model provided a value of

[26] Estimated Environmental Concentrations

0.59 μg/L to evaluate the risk to human health. This value represents the ground water concentration of oxadiazon at the maximum allowable rate (2 applications/year of 4lb. ai/acre). It also assumes that the ground water is exceptionally vulnerable to contamination. This estimate is applied to all exposure scenarios regardless of the duration of exposure since SCI-GROW calculates only the 90-day average value.

4.3 Occupational Exposure

HED has determined that there are potential exposures to mixers, loaders, applicators, or other handlers during standard use-patterns associated with oxadiazon. Although postapplication contact of workers with oxadiazon is minimal, the Agency has ascertained that there are potential postapplication exposures to individuals re-entering treated areas associated with mowing and harvesting.

4.3.1 Handler

The Agency has found that occupational exposure to oxadiazon via the dermal and inhalation routes of exposure may occur during mixing, loading and applying through the use of ground spray, granular and other lawn application methods. Based on the use patterns, 14 major occupational exposure scenarios were identified for oxadiazon: (1a) mixing/loading wettable powders for chemigation application; (1b) mixing/loading wettable powders for groundboom application; (1c) mixing/loading wettable powders for rights-of-way sprayer; (2) loading granular formulations; (3) applying with a groundboom; (4) applying with a rights-of-way sprayer; (5) applying wettable powders for handgun applicators (ORETF)[27]; (6) applying granular with a tractor drawn spreader; (7) backpack sprayer (LCO)[28]; (8) low pressure handwand-wettable powder formulations (LCO); (9) high pressure-handwand-wettable powder formulations (LCO); (10) lawn handgun-wettable powder formulations (ORETF); (11) granulars with a push type spreader (ORETF) and (12) granulars with a bellygrinder (LCO). Typical application rates for oxadiazon range from 3 to 4 lb. ai/acre, with the higher rate being applied to golf courses, roadside turf, lawns, parks, recreational areas and woody ornamentals.

Since the use patterns for oxadiazon do not suggest any long term use, exposure scenarios of a longer duration were not considered. The exposure scenarios are of short-term (1-7 days) and intermediate-term (1 week to several months). The estimated exposures considered baseline protection (long pants, long shirts and no gloves - dermal; no respirator - inhalation), additional PPE (long pants, long shirts and chemical resistant gloves and/or double layer of clothing - dermal; all of the dermal protection plus 80% protection from dust/mist respirator - inhalation), and engineering controls (use of water soluble packages). Handler exposure assessments were completed by EPA using baseline exposure scenarios previously noted and, if required, increasing levels of risk mitigation (PPE and

[27] Outdoor Residential Exposure Task Force

[28] Lawn Care Operator

engineering controls) to achieve **an MOE of 100 for non-cancer risks. For cancer, there is a concern for risk estimates >1.0x 10^{-4}.**

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of the reregistration of oxadiazon. In such instances, it is the policy of the HED to use data from the PHED[29] Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available. HED's level of confidence in these data are shown in the occupational and residential exposure assessment and recommendations for oxadiazon (Tadayon, 2001).

4.3.1.1 Noncancer Handler Exposure/Risks

The short-term and intermediate-term MOEs for dermal and inhalation exposures were calculated using an oral NOAEL of 12 mg/kg/day for both exposure durations (see Section 3.3 Dose Response Assessment). The Agency also used route-to-route extrapolations from this oral study for both exposure assessments. A dermal absorption rate of 9% was applied to the dermal exposure assessments and an inhalation absorption rate of 100% was applied to the inhalation exposure assessments.

The results of the **short and intermediate-term handler** assessments are presented in Table 5 and indicate that all potential non-cancer exposure scenarios provide at least one application rate with a total MOE(s) greater than or equal to 100 at either the **baseline** (i.e., long pants, long sleeved shirts, no gloves) using open systems**, PPE** (i.e., long pants, long sleeved shirts, and chemical resistant gloves while using open systems) or using **engineering controls** (i.e., closed systems). The only exception, with the feasible level of mitigation, is scenario 8 (low pressure handwand-wettable powder formulations). As further shown, dermal exposure rather than inhalation exposure drives the total MOE for scenario 8 as well as the majority of cases. Total MOEs for all scenarios range from 2 to 3000 and 37 MOEs were calculated for the various application rates. **The data show that baseline or mitigation measures raised the MOEs to values greater than or equal to 100 for all scenarios except scenario 8.**

[29] Pesticide Handlers Exposure Database

Table 5: Exposure Variables (Noncancer), MOEs for Uses of Oxadiazon												
Exposure Scenario (Scenario #)	Crop Type	App Rates (lb ai/acre)	Daily Acres Treated	Dermal MOEs			Inhalation MOEs			Total MOEs		
				Base line	PPE	Eng. Control	Base line	PPE	Eng. Control	Base line	PPE	Eng. Control
Mixer/Loader												
Mixing/Loading Wettable Powders for Chemigation Application (1a)	sod farms	3	350	2	59	780	16	80	2900	2	35	610
Mixing/Loading Wettable Powders for Groundboom Application (1b)	conifer nurseries, woody ornamentals	4	40	14	380	NA	100	520	NA	12	220	NA
	herbaceous ornamentals	3	40	18	510	NA	140	700	NA	16	300	NA
	sod farms	3	80	9	260	NA	70	350	NA	8	150	NA
	golf courses	4	40	14	380	NA	100	520	NA	12	220	NA
Mixing/Loading Wettable Powders for Rights-of-Way Sprayer (1c)	roadside turf, ornamentals	4	40	14	380	NA	100	520	NA	12	220	NA
Loading Granular formulations (2)	sod farms, conifers forest	4	80	3000	NA	NA	1300	NA	NA	920	NA	NA
	golf course turf, parks, recreational areas	4	40	6000	NA	NA	2600	NA	NA	1800	NA	NA
	woody ornamentals	4	40	6000	NA	NA	2600	NA	NA	1800	NA	NA
Applicator												
Applying with a Groundboom (3)	sod farms	3	80	2400	NA	NA	4100	NA	NA	1500	NA	NA
	herbaceous ornamentals	3	40	4800	NA	NA	8100	NA	NA	3000	NA	NA
	golf courses		40	3600	NA	NA	6100	NA	NA	2300	NA	NA
	conifer nurseries, woody ornamentals	4	40	3600	NA	NA	6100	NA	NA	2300	NA	NA
Applying with a Rights-of-Way Sprayer (4)	roadsides	4	40	38	130	NA	1200	1200	NA	37	120	NA

Table 5: Exposure Variables (Noncancer), MOEs for Uses of Oxadiazon												
Exposure Scenario (Scenario #)	Crop Type	App Rates (lb ai/acre)	Daily Acres Treated	Dermal MOEs			Inhalation MOEs			Total MOEs		
				Base line	PPE	Eng. Control	Base line	PPE	Eng. Control	Base line	PPE	Eng. Control
Applying Wettable-Powders for Handgun Applicators (ORETF) (5)	lawns, parks, recreational areas	4	5	See PPE	550	NA	36000	36000	NA	See PPE	540	NA
Applying Granular with a Tractor Drawn Spreader (6)	sod farms	4	80	2500	NA	NA	1900	NA	NA	1100	NA	NA
	golf courses	4	40	5100	NA	NA	3800	NA	NA	2200	NA	NA
Mixer/Loader/Applicator												
Backpack Sprayer (LCO) (7)	lawns, golf courses, ornamentals nurseries	4	5	See PPE	160	NA	1200	1200	NA	See PPE	140	NA
Low Pressure Handwand - Wettable Powder Formulations (LCO) (8)	lawns, golf courses, nursery stock	4	5	14	65	NF	33	160	NF	10	46	NF
High Pressure Handwand -- (Wettable Powder Formulations) (9)	woody ornamentals, conifer nurseries.	4	5	See PPE	160	NA	300	300	NA	See PPE	100	NA
Lawn Handgun (Wettable Powder Formulations) (ORETF) (10)	ornamentals, lawns, parks rec areas	4	5	560	NA	NA	580	NA	NA	280	NA	NA
Granulars with a Push Type Spreader (ORETF) (11)	lawns, golf courses, parks, recreational areas, ornamentals	4	5	1100	NA	NA	4800000	NA	NA	1100	NA	NA
Granulars with a Bellygrinder (LCO) (12)	golf courses, parks, rec areas.	4	1	200	NA	NA	2900	NA	NA	190	NA	NA

Baseline dermal unit exposure scenarios includes long pants, long shirts and no gloves.
Baseline inhalation unit exposure represents no respirator
PPE dermal unit exposure includes long pants, long shirts and gloves for scenarios 5, 7, and 9.
PPE dermal unit exposure includes long pants, long shirts gloves and double layer (50% protection) for scenarios 1a, 1b, 1c, and 8.
PPE inhalation unit exposure represents dust/ mist respirator (80 % protection) for scenarios 1a, 1b, 1c, and 8.
Engineering Control dermal unit exposure scenarios includes long pants, long shirts, gloves and water soluble packages for scenario 1a.

Engineering inhalation unit exposure represents no respirator. NA = Not applicable NF = Not Feasible

4.3.1.2 Cancer Handler Exposure/Risks

The cancer risk assessments for handlers used baseline exposure scenarios and, as needed, increasing levels of risk mitigation (PPE and engineering) to achieve cancer risks that would be considered of no concern. According to Agency policy[30], acceptable cancer risks for occupational exposure to pesticides varies from 1×10^{-4} to 1×10^{-6}, depending on the course of action taken by the Agency as outlined in the policy memo on this subject. The Q_1* used in this risk assessment is 7.11×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents (see Section 3.3 Dose Response Assessment).

Potential cancer risks (LADD[31]) to handlers were assessed using the following assumptions:

- The average body weight of 70 kg is used, representing a typical adult.
- Career duration is assumed to be 35 years. This represents a typical working lifetime.
- Lifetime is assumed to be 70 years.
- Dermal absorption is assumed to be 9%, and inhalation absorption is assumed to be 100% of the oral dose. The dermal and inhalation doses were added together to represent total daily dose.

In addition, two exposure frequencies were used in the calculations, the first represented the maximum number of applications per site per season to represent private use (3), and the second frequency applied a factor of ten to the first frequency to represent commercial handlers making multiple applications per site per season (30).

The results of the **short and intermediate-term handler** cancer assessments presented in Table 6 indicate that values range from 1.65E-2 to 4.66E-7 at the baseline (long pants, long shirts and no gloves), 2.56E-3 to 4.11E-7 at PPE1 (long pants, long shirts, gloves and no respirator), 2.40E-3 to 3.51

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[30] The Agency has defined a range of acceptable cancer risks based on a policy memorandum dated August 14, 1996, by then Office of Pesticide Programs Director Dan Barolo. This memo refers to a predetermined quantified "level of concern" for occupational carcinogenic risk. Occupational carcinogenic risks that are 1×10^{-6} or lower require no risk management action. For those chemicals subject to reregistration, the Agency is carefully examining uses with estimated risks in the 10^{-6} to 10^{-4} range to seek ways of cost-effectively reducing risks. If carcinogenic risks are in this range for occupational handlers, increased levels of personal protection are warranted as is commonly applied with noncancer risk estimates (e.g., additional PPE or engineering controls). Carcinogenic risks that remain above 1.0×10^{-4} at the highest level of mitigation appropriate for that scenario remain a concern.

[31] Lifetime Average Daily Dose

E-7 at PPE2 (long pants, long shirts, double layer, gloves and no respirator), 1.05E-3 to 1.98E-7 at PPE3

Table 6: Exposure Variables for Handlers with Baseline Exposure Scenarios and Increasing Levels of Risk Mitigation (Cancer) for Uses of Oxadiazon									
Exposure Scenario (Scenario #)	Crop/Target	Appl Rates (lb ai/acre)	Daily Acres Treated	Cancer					
				Base line	PPE 1	PPE 2	PPE 3	PPE 4	Eng. Control
Mixer/Loader									
Mixing/Loading Wettable Powders for Chemigation Application (1a)	sod farms	3	350	1.65e-03/ 1.65e-02	2.56e-04/ 2.56e-03	2.40e-04/ 2.40e-03	1.05e-04/ 1.05e-03	8.90e-05/ 8.90e-04	4.92e-06/ 4.92e-05
Mixing/Loading Wettable Powders for Groundboom Application (1b)	conifer nurseries, woody ornamentals	4	40	2.51e-04/ 2.51e-03	3.89e-05/ 3.89e-04	3.65e-05/ 3.65e-04	1.60e-05/ 1.60e-04	1.36e-05/ 1.36e-04	7.49e-07/ 7.49e-06
	herbaceous ornamentals	3	40	1.88e-04/ 1.88e-03	2.92e-05/ 2.92e-04	2.74e-05/ 2.74e-04	1.20e-05/ 1.20e-04	1.02e-05/ 1.02e-04	5.62e-07/ 5.62e-06
	sod farms	3	80	3.77e-04/ 3.77e-03	5.84e-05/ 5.84e-04	5.48e-05/ 5.48e-04	2.39e-05/ 2.39e-04	2.03e-05/ 2.03e-04	1.12e-06/ 1.12e-05
	golf courses	4	40	2.51e-04/ 2.51e-03	3.89e-05/ 3.89e-04	3.65e-05/ 3.65e-04	1.60e-05/ 1.60e-04	1.36e-05/ 1.36e-04	7.49e-07/ 7.49e-06
Mixing/Loading Wettable Powders for Rights-of-Way Sprayer (1c)	roadside turf, ornamentals	4	40	2.51e-04/ 2.51e-03	3.89e-05/ 3.89e-04	3.65e-05/ 3.65e-04	1.60e-05/ 1.60e-04	1.36e-05/ 1.36e-04	7.49e-07/ 7.49e-06
Loading Granular formulations (2)	sod farms, conifers forest	4	80	3.28e-06/ 3.28e-05	3.10e-06/ 3.10e-05	2.68e-06/ 2.68e-05	1.28e-06/ 1.28e-05	8.63e-07/ 8.63e-06	2.20e-08/ 2.20e-07
	golf course turf, parks, recreational areas	4	40	1.64e-06/ 1.64e-05	1.55e-06/ 1.55e-05	1.34e-06/ 1.34e-05	6.42e-07/ 6.42e-06	4.31e-07/ 4.31e-06	1.10e-08/ 1.10e-07
	woody ornamentals	4	40	1.64e-06/ 1.64e-05	1.55e-06/ 1.55e-05	1.34e-06/ 1.34e-05	6.42e-07/ 6.42e-06	4.31e-07/ 4.31e-06	3.29e-08/ 3.29e-07
Applicator									
Applying with a Groundboom (3)	sod farms	3	80	2.00e-06/ 2.00e-05	2.00e-06/ 2.00e-05	1.73e-06/ 1.73e-05	1.41e-06/ 1.41e-05	1.14e-06/ 1.14e-05	4.94e-07/ 4.94e-06

Table 6: Exposure Variables for Handlers with Baseline Exposure Scenarios and Increasing Levels of Risk Mitigation (Cancer) for Uses of Oxadiazon									
Exposure Scenario (Scenario #)	Crop/Target	Appl Rates (lb ai/acre)	Daily Acres Treated	Cancer					
				Base line	PPE 1	PPE 2	PPE 3	PPE 4	Eng. Control
	herbaceous ornamentals	3	40	1.00e-06/ 1.00e-05	1.00e-06/ 1.00e-05	8.67e-07/ 8.67e-06	7.06e-07/ 7.06e-06	5.71e-07/ 5.71e-06	2.47e-07/ 2.47e-06
	golf courses		40	1.34e-06/ 1.34e-05	1.34e-06/ 1.34e-05	1.16e-06/ 1.16e-05	9.42e-07/ 9.42e-06	7.61e-07/ 7.61e-06	3.29e-07/ 3.29e-06
	conifer nurseries, woody ornamentals	4	40	1.34e-06/ 1.34e-05	1.34e-06/ 1.34e-05	1.16e-06/ 1.16e-05	9.42e-07/ 9.42e-06	7.61e-07/ 7.61e-06	3.29e-07/ 3.29e-06
Applying with a Rights-of-Way Sprayer (4)	roadsides	4	40	8.07e-05/ 8.07e-04	2.60e-05/ 2.60e-04	2.00e-05/ 2.00e-04	2.40e-05/ 2.40e-04	1.80e-05/ 1.80e-04	NA
Applying Wettable-Powders for Handgun Applicators (ORETF) (5)	lawns, parks, recreational areas	4	5	See PPE	5.57e-06/ 5.57e-05	2.94e-06/ 2.94e-05	5.50e-06/ 5.50e-05	2.87e-06/ 2.87e-05	NA
Applying Granular with a Tractor Drawn Spreader (6)	sod farms	4	80	9.31e-07/ 9.31e-06	8.23e-07/ 8.23e-05	7.03e-07/ 7.03e-06	3.95e-07/ 3.95e-06	2.75e-07/ 2.75e-06	1.82e-07/ 1.82e-06
	golf courses	4	40	4.66e-07/ 4.66e-06	4.11e-07/ 4.11e-06	3.51e-07/ 3.51e-06	1.98e-07/ 1.98e-06	1.38e-07/ 1.38e-06	9.11e-08/ 9.11e-07
Mixer/Loader/Applicator									
Backpack Sprayer (LCO) (7)	lawns, golf courses, ornamentals nurseries	4	5	See PPE	2.13e-05/ 2.13e-04	1.45e-05/ 1.45e-04	1.93e-05/ 1.93e-04	1.25e-05/ 1.25e-04	NA

Table 6: Exposure Variables for Handlers with Baseline Exposure Scenarios and Increasing Levels of Risk Mitigation (Cancer) for Uses of Oxadiazon									
Exposure Scenario (Scenario #)	Crop/Target	Appl Rates (lb ai/acre)	Daily Acres Treated	Cancer					
				Base line	PPE 1	PPE 2	PPE 3	PPE 4	Eng. Control
Low Pressure Handwand - Wettable Powder Formulations (LCO) (8)	lawns, golf courses, nursery stock	4	5	3.10e-04/ 3.10e-03	1.56e-04/ 1.56e-03	1.38e-04/ 1.38e-03	8.30e-05/ 8.30e-04	6.50e-05/ 6.50e-04	NA
High Pressure Handwand -- (Wettable Powder Formulations) (9)	woody ornamentals, conifer nurseries.	4	5	See PPE	1.88e05/ 1.88e-04	1.20e-05/ 1.20e-04	1.98e-05/ 1.98e-04	1.31e-05/ 1.31e-04	NA
Lawn Handgun (Wettable Powder Formulations) (ORETF) (10)	ornamentals, lawns, parks rec areas	4	5	1.06e-05/ 1.06e-04	1.06e-05/ 1.06e-04	8.03e-06/ 8.03e-05	6.44e-06/ 6.44e-05	3.89e-06/ 3.89e-05	NA
Granulars with a Push Type Spreader (ORETF) (11)	lawns, golf courses, parks, recreational areas, ornamentals	4	5	2.33e-06/ 2.33e-05	1.80e-06/ 1.80e-05	No data	1.80e-06/ 1.80e-05	No data	NA
Granulars with a Bellygrinder (LCO) (12)	golf courses, parks, rec areas.	4	1	1.61e-05/ 1.61e-04	1.50e-05/ 1.50e-04	9.60e-06/ 9.60e-05	1.42e-05/ 1.42e-04	8.77e-06/ 8.77e-05	NA

Baseline dermal unit exposure scenarios includes long pants, long shirts and no gloves.
PPE 1 cancer risk includes long pants, long shirts, gloves and no respirator.

PPE 2 cancer risk includes long pants, long shirts, double layer, gloves and no respirator.
PPE 3 cancer risk includes long pants, long shirts, gloves and respirator.
PPE 4 cancer risk includes long pants, long shirts, double layer, gloves and respirator.
Engineering Control dermal unit exposure scenarios includes long pants, long shirts, gloves and water soluble packages.
Engineering inhalation unit exposure represents no respirator.

(long pants, long shirts, gloves and respirator), 8.90E-4 to 1.38E-07 at PPE4 (long pants, long shirts, double layer, gloves and respirator) and 4.92E-5 to 1.10E-8 at engineering control. **Overall, these data show that none of the evaluated scenarios have cancer risks that exceed 1.00E-4 at the highest feasible level of mitigation.**

4.3.2 Occupational Postapplication

HED uses the term "post-application" to describe those individuals who can be exposed to pesticides after entering areas previously treated with pesticides and performing certain jobs, tasks or activities (also often referred to as reentry exposure). Most of the oxadiazon used in agriculture is applied either pre-plant or when the crops are quite small (early post-emergence). This information together with the degree of mechanization minimizes the postapplication contact of workers with oxadiazon. Nevertheless, the Agency has determined that there are potential postapplication exposures to individuals re-entering oxadiazon treated areas for the purpose of:

c. *Roadsides*: mowing
d. *Bermuda grass rights-of-way*: mowing
e. *Sod farms*: mowing and harvesting
f. *Golf-course turfgrass*: mowing

4.3.2.1 Data Sources and Assumptions for Scenarios Considered

Based on data submitted for reregistration, it can be assumed that the most common postapplication exposures will occur for workers on turf. Based on label restrictions and patterns of use, oxadiazon is applied early in the season, either pre-plant or before weeds emerge (pre-emergence). Mowing would be a common postapplication activity after either spraying method. Treated turf or grasses will routinely require reentry activities, such as mowing and watering, and eventually harvesting in the case of sod farms. Although two transferable turf residue (TTR) studies and one Jazzercize study (MRID No. 43517801) were submitted in support of the reregistration of oxadiazon, only the Jazzercize study was found to be acceptable for this assessment because the TTR values obtained from the two TTR studies were less than 1%. TTR values less than 1% are not considered acceptable by HED since the submitted studies were performed with a modified California Cloth Roller sampling device, which has been replaced with new equipment accredited by ORETF. TTR values derived from a modified California Cloth Roller sampling device can be used if accompanied by concurrent transfer coefficient measurements. This was not the case for oxadiazon.

The TTR value from the Jazzercise study utilized a wettable powder formulation which by far has a higher potential for exposure than the oxadiazon granular formulations. Since a majority of the total use involves granular formulations, using wettable powder TTR values is a conservative approach and can be considered the upper level estimates of exposure.

A linear regression to calculate a dissipation rate (T½) for oxadiazon TTR from irrigated and non-irrigated test sites was performed, using all non-zero, uncorrected, averaged data point from DAT-0

through DAT-7. Calculated dissipation half-lives for the irrigated plot was 1.7days (R^2=0.64) and for the non- irrigated plot was 1.4 days (R^2=0.64)

Because oxadiazon has a low vapor pressure (1.0 x 10^{-6}mm Hg) and is only used outdoors, the inhalation component of postapplication exposure is anticipated to be negligible. **Therefore, all calculations of postapplication risk estimates have been done for dermal exposure only, and there was no need to aggregate postapplication exposure routes for workers.**

4.3.2.2 Postapplication Exposure Risk Estimates

For turf or sod mowing and harvesting, transfer coefficients of 500 and 16,500 cm^2/hr were used, based on the ARTF [32] data. The TTR values are assumed to be 5% of the application rate on Day 0 for turfgrass application (the 5% rate for turfgrass in the high end of the values observed in the studies of Hurto and Prinster, 1993; Goh *et al.,* 1986 and Cowell *et al., 1993*). **As shown in Table 7, short and intermediate-term exposures for noncancer risks had estimated MOEs of 300-10,000, which exceed the target value of 100. Similarly, occupational postapplication cancer risks were estimated to fall within the acceptable range of 1 x 10^{-4} to 1 x 10^{-6}.**

4.3.3 Non-Occupational Postapplication Exposures and Risk

The Agency has determined that there are potential postapplication exposures to residents entering oxadiazon treated lawns, either as a result of commercial or private application. The scenarios likely to result in postapplication exposures are:

- dermal postapplication risks to adults and toddlers (defined as 5<12 years old and considered by HED to be the most sensitive subpopulation of children) when entering oxadiazon-treated turf and lawns;

- oral postapplication risks to toddlers from "hand-to-mouth" (*i.e.*, ingestion of grass, soil, granular pellets, or hand-to-mouth contact) exposure when reentering lawns treated with granular and wettable powder formulations.

Representative turf reentry activities include, but are not limited to:

(1) Adults involved in a low exposure activity, such as golfing or walking on treated turf.
(2) Toddlers involved in a low exposure activity, such as walking on treated turf.
(3) Adults mowing or other moderate contact activity, for 1-2 hours.
(4) Adults involved in a high exposure activity, such as heavy yard work (doses similar to occupational scenarios for cutting and harvesting sod)**.**
(5) Toddlers involved in high exposure activities on turf.

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[32] Agricultural Reentry Task Force

Table 7: Occupational Short- and Intermediate-Term Postapplication Risks for Oxadiazon at Day 0							
Crop/Use Pattern	**Application Rate (lb ai/acre)**	**Postapplication Activity**	**Transfer Coefficient[a]**	**Short Term and Intermediate Term Risks**		**Cancer Risk**	
				TTR[b] (μg/cm^2)	**MOE[c]**	**LADD[d] mg/kg/day**	**Risk[e]**
Golf Course Turf	**4**	**Mow, seed, scout, mechanical weed, aerate, fertilize, prune**	**500**	**0.2 (5% of application rate)**	**10,000**	**4.23e-6**	**3.01e-7**
		Transplant, hand weed	**16,500**		**300**	**1.39e-4**	**9.92e-6**
Sod Farms	**4**	**Mow, scout, mechanical weed, irrigate**	**500**		**10,000**	**4.23e-6**	**3.01e-7**
		Transplant, hand weed, harvest (hand or mechanical)	**16,500**		**300**	**1.39e-4**	**9.92e-6**
Bermuda Grass Rights of Way	**4**	**Mow, seed, scout, mechanical weed, aerate, fertilize**	**500**		**10,000**	**4.23e-6**	**3.01e-7**

[a] Transfer coefficient from Science Advisory Council for Exposure: Policy Memo # 003 .1 "Agricultural Transfer Coefficients," Revised - August 7, 2000.

[b] TTR source: 5% of application rate, "Residential SOP Revised February 2001 " was used for determination of MOE's.

[c] MOE = Short-term NOAEL (12 mg/kg/day; based on a dermal study) / dermal dose where absorbed dose = TTR (μg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time(8hrs/day)x dermal absorption (9 %) / body weight (60 kg; adult).

[d] Absorbed dermal dose where absorbed dose = TTR (μg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (8 hrs/day) x dermal absorption (9 %) / body weight (70 kg) x (Number of days (3) exposure per year applicator) /365 days per year) x 35 years worked/70 year lifetime

[e] Cancer Risk = LADD (mg/kg/day) x (Q_1*), where Q_1* = 7.11e^{-2} (mg/kg/day)$^{-1}$.

Note: TTR - Turf Transferable Residue

4.3.3.1 Non-occupational Postapplication Dermal Exposure (Adults and Toddlers)

4.3.3.1.1 Data Sources and Assumptions for Scenarios Considered

A turf re-entry exposure study (Jazzercise study), using a spray application, was mentioned in the Occupational Postapplication section (see Section 4.3.2, Occupational Postapplication). As the study was found to be acceptable for the risk assessment, the highest mean residues were also used to estimate short-term (DAT 0-1) for irrigated and non-irrigated plots evaluated for these scenarios.

The duration of postapplication dermal exposure is expected to be either short-term or intermediate-term, based on oxadiazon turf residue dissipation data. The short-term and intermediate-term MOEs for dermal exposures were calculated using an oral NOAEL of 12 mg/kg/day with a dermal absorption rate of 9%; this value was derived from the same study used for the occupational handler noncancer exposures (see 4.3.1.1, Noncancer Handler Exposure/Risks). For the cancer risk estimates, the Q_1* of 7.11 x 10^{-2} $(mg/kg/day)^{-1}$ in human equivalents (see 4.3.1.2, Cancer Handler Exposure/Risks) was used.

As calculated from the previously discussed Jazzercise study, oxadiazon has a half-life on turf of up to 1.4 days (irrigated) and 1.7 days (non-irrigated) after spraying, requiring several days to dissipate to non detectable levels of transferable residues. Because the label prohibits application more than 3 times per year, and even with the slow dissipation rates, it is not expected that individual residential exposure duration would exceed 30 days in duration. Exposure on a residential lawn would diminish continuously with time, while exposure through recreation turf contact would more likely be random, intermittent events of varying doses, all less than the dose predicted in this assessment. Residential postapplication exposure assessments assumed residents wear the following attire: short sleeved shirt, short pants, shoes and socks, and no gloves or respirator. **As stated earlier, negligible oxadiazon inhalation exposure is anticipated for non-handlers, due to the low chemical vapor pressure and the dilution of the vapor outdoors.** Other assumptions and all equations used for the assessment of each exposure scenario can be found in the occupational and residential exposure assessment and recommendations for oxadiazon document (Tadayon, 2001).

Dermal postapplication exposure estimates were conducted using the highest mean postapplication residue to estimate short-term DAT 0-1 for irrigated and non-irrigated plots from the previously discussed Jazzercise study (wettable powder formulations). The dermal transfer coefficients from the Jazzercize study (MRID No. 43517801) and the revised residential SOPs were also used. As the study was found to be acceptable for the risk assessment.

4.3.3.1.2 Non-occupational Postapplication Dermal Exposure Risk Estimates

Utilizing the Jazzercize wettable powder application study residue data and revised residential SOPs, **all of the non-cancer risks scenario developed for adults and toddlers had short-term and intermediate-term dermal MOEs greater than 100. The cancer risks for all adult residential**

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dermal postapplication exposure were between 6.22×10^{-6} to 7.51×10^{-8}. The resulting risk estimates are summarized in **Tables 8 and 9.**

4.3.3.2 Incidental Oral Exposure for Toddlers

Only limited information was received regarding the size and distribution of granular formulations. This information would help to refine or characterize the estimate of potential risk from episodic incidental ingestion of granules beyond the current screening level. If the particles are very fine, individual grains would be difficult to pick up, or even to see when applied on a lawn. If used according to label directions, it is unlikely that oxadiazon granules would be accessible to a child. However, larger granules or pellets of a few millimeters diameter might be attractive and easily picked up by a toddler.

An intermediate-term (7-30 days) MOE was not calculated since exposure by this route for weeks is considered less likely to occur than short-term (1-7days) exposure. Similarly, there was no indication from the studies in the database that toxic effects observed over the short-term would be any different over a longer term exposure. Estimated incidental oral short-term exposures ("hand-to-mouth") for toddlers had an MOE of 100 using the TTR default values from the residential SOP; when the TTR data from submitted oxadiazon study were used, the MOEs were 90 and 240 **(Table 10**). The former MOE of 90 does not exceed the target value, however, the submitted study TTR data were from the wettable powder formulation and the major formulation used is granular oxadiazon. It is probable, therefore, that the risk indicated for irrigated dormant grass is an overestimate and not likely to be a cause for concern (also see Section 4.3.3.1, Data Sources and Assumptions for Scenarios Considered). MOEs were not calculated for the incidental ingestion of oxadiazon granules because an acute RfD was not selected for this non-food use pesticide. Additionally, there is no indication from the studies in the guideline database that a single oral administration of oxadiazon presents a hazard. This statement is also supported by the high rat acute LD_{50} for oxadiazon (>5000 mg/kg). It is thought, therefore, that the incidental ingestion of granules is not likely to be a cause for concern.

It is considered reasonably likely that dermal and oral incidental exposures may occur in the same day for children playing on an oxadiazon-treated lawn. **However, these exposures were not aggregated due to the short-term hand-to-mouth exposures having MOEs less than or equal to the target MOE of 100.** Because an exposure just mets or exceeds the level of concern by a single route, that route must be mitigated prior to aggregating exposures by other routes otherwise, the reported risk is only increased.

Table 8. Residential Dermal Postapplication Non-Cancer Risks for Oxadiazon

Dermal Scenarios	Application Rate (lb ai/acre)	Exposure Time (hours/day)	Short Term and Intermediate Term Risks									
			Transfer Coefficient (cm^2/hr)[a]	Transfer Coefficient (cm^2/hr) Irrigated[b]	Transfer Coefficient (cm^2/hr) Non-Irrigated[c]	TTR[d] (ug/cm^2) DAT 0-1	Dermal Dose (mg/kg/day)[e]	Dermal Dose (mg/kg/day) Irrigated[f]	Dermal Dose (mg/kg/day) Non-Irrigated[g]	MOEs[h]	MOEs[i] Irrigated	MOEs[j] Non-Irrigated
Adult dermal turf contact	4	2	14500	4300	7,400	1.53	NA	1.97e-2	3.40e-2	NA	610	350
						2.0	8.70e-2	NA	NA	140	NA	NA
Toddler dermal turf contact		2	5200	1600	2,700	0.87	NA	1.67e-2	2.82e-2	NA	720	430
						2.0	3.12e-2	NA	NA	390	NA	NA
Adult walking, playing golf		4	500	NA	NA	2.0	6.0e-3	NA	NA	2000	NA	NA
Adult push mowing lawn		2	500	NA	NA	2.0	3.0e-3	NA	NA	4000	NA	NA

a Transfer coefficient from the Residential SOP's (2/01) used for fresh grass

b Transfer coefficient from turf study MRID # 435178-01used for dormant grass

c Transfer coefficient from turf study MRID # 435178-01used for dormant grass

d TTR source: wettable powder from turf studies MRID # 435178-01, DAT 0-1 residue **or** residential SOP (5% application rate)

e Dermal dose (mg/kg/day) = TTR (5% application rate) (μg/cm^2) x TC (from residential SOP,s) (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (2 or 4hrs/day) x dermal absorption (9 %) / body weight (60 kg adult or 15 kg toddler).

f Dermal dose (mg/kg/day) irrigated = TTR (from MRID #435178-01) (μg/cm^2) x TC (MRID #435178-01) (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (2 hrs/day) x dermal absorption (9 %)/ body weight (60 kg adult or 15 kg toddler).

g Dermal dose (mg/kg/day) non-irrigated = TTR (from MRID #435178-01) (μg/cm^2) x TC (MRID #435178-01) (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (2 hrs/day) x dermal absorption (9 %) / body weight (60 kg adult or 15 kg toddler).

h MOE = Short-term NOAEL (12 mg/kg/day; based on an oral study) / dermal dose (mg/kg/day)

i MOE (irrigated) = Short-term NOAEL (12 mg/kg/day; based on an oral study) / dermal dose (mg/kg/day)

j MOE (non-irrigated) = Short-term NOAEL (12 mg/kg/day; based on an oral study) / dermal dose (mg/kg/day)

Note: TTR - Turf Transferable Residue rounded to 2.0 ug/cm^2

Table 9. Residential Dermal Postapplication Cancer Risks for Oxadiazon

Dermal Scenarios	Application Rate (lb ai/acre)	Exposure Time (hours/day)	Transfer Coefficient (cm^2/hr)[a]	Transfer Coefficient (cm^2/hr) Irrigated[b]	Transfer Coefficient (cm^2/hr) Non-Irrigated[c]	TTR[d] (ug/cm^2) DAT 0-1	LADD[e] mg/kg/day	LADD[f] mg/kg/day irrigated	LADD[g] mg/kg/day[f] Non-Irrigated	Cancer Risk[h]	Cancer Risk Irrigated[j]	Cancer Risk Non-irrigated[j]
Adult dermal turf contact	4	2	14500	4300	7400	1.53	NA	6.95e-5	1.2e-4	NA	3.62e-6	6.22e-6
						2.0	3.06e-04	NA	NA	1.59e-5	NA	NA
Toddler dermal turf contact		2	5200	1600	2700	0.87	NF	NF	NF	NF	NF	NF
						2.0	NF	NF	NF	NF	NF	NF
Adult walking, playing golf		4	500	NA	NA	2.0	2.11e-5	NA	NA	1.50e-6	NA	NA
Adult push mowing lawn		2	500	NA	NA	2.0	1.06e-5	NA	NA	7.51e-7	NA	NA

a Transfer coefficient from the Residential SOP's (2/01) used for fresh grass
b Transfer coefficient from turf study MRID # 435178-01used for dormant grass
c Transfer coefficient from turf study MRID # 435178-01used for dormant grass
d TTR source: wettable powder and granular turf studies MRID # 435178-01, DAT 0-1 residue
e LADD (mg/kg/day) = TTR (μg/cm^2)(5% of application rate) x TC(residential SOP) (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (2 or 4 hrs/day) x dermal absorption (9 %) / body weight (70 kg) x (Number of days (3) exposure per year applicator) /365 days per year) x 35 years worked/70 year lifetime
f LADD (mg/kg/day)(irrigated) = TTR (μg/cm^2) (from MRID # 435178-01) x TC (cm^2/hr)(from MRID # 435178-01) x conversion factor (1 mg/1,000 μg) x exposure time (2 hrs/day) x dermal absorption (9 %) / body weight (70 kg) x (Number of days (3) exposure per year applicator) /365 days per year) x 35 years worked/70 year lifetime
g LADD (mg/kg/day)(non-irrigated) = TTR (μg/cm^2)(from MRID # 435178-01) x TC(from MRID #435178-01) (cm^2/hr) x conversion factor (1 mg/1,000 μg) x exposure time (2 hrs/day) x dermal absorption (9 %) / body weight (70 kg) x (Number of days (3) exposure per year applicator) /365 days per year) x 35 years worked/70 year lifetime
h Cancer Risk = LADD (mg/kg/day) x (Q_1*), where $Q_1^* = 7.11e^{-2}$ $(mg/kg/day)^{-1}$.
i Cancer Risk (irrigated) = LADD (mg/kg/day) (irrigated) x (Q_1*), where $Q_1^* = 7.11e^{-2}$ $(mg/kg/day)^{-1}$.
j Cancer Risk (non-irrigated) = LADD (mg/kg/day)(non-irrigated) x (Q_1*), where $Q_1^* = 7.11e^{-2}$ $(mg/kg/day)^{-1}$.

NA= Not applicable
NF= Not Feasible

Note: TTR - Turf Transferable Residue rounded to 2.0 ug/cm^2

Table 10 Residential Oral Nondietary Postapplication Risks to Toddlers from "Hand-to-Mouth" and Ingestion Exposure When Reentering Lawns Treated with Granular or wettable powder Oxadiazon Formulations

Type of Exposure	Application Rate[a] (lb ai/acre)	Ingestion Rate or Other Assumptions[b]	Short-Term		
			TTR[c] (μg/cm^2) DAT 0-1	Oral Dose[d] (mg/kg/day)	MOE[e]
Hand to Mouth Activity	4	20 cm^2/event surface area of 1-3 fingers; 20 events/hr; fresh grass 5% of ai dislodgeable with potentially wet hands	2.0	1.19e-01	100
		20 cm^2/event surface area of 1-3 fingers; 20 events/hr; 2.1% of ai dislodgeable with potentially wet hands (dormant grass, irrigated)	1.0	5.02e-02	240
		20 cm^2/event surface area of 1-3 fingers; 20 events/hr; 5.5% of ai dislodgeable with potentially wet hands (dormant grass, non- irrigated)	2.5	1.31e-01	90
Incidental Turfgrass Ingestion		25 cm^2/day of turf 20% application rate (residential SOP) fresh grass	9.0	1.49e-02	805
		25 cm^2/day of turf Irrigated (MRID # 435178-01) used for dormant grass	0.87	2.60e-03	4700
		25 cm^2/day of turf Non-Irrigated(MRID # 435178-01)used for dormant grass	1.53	1.45e-03	8300
Incidental Ingestion of Soil		100 mg/day ingestion; 0.67 cm^3/gm soil	NA	2.12e-04	57000

a Application rates represent maximum label rates from current EPA registered labels.

b Assumptions from Residential SOP's (February, 2001). fresh grass

c TTR source: wettable powder and granular oxadiazon turf studies MRID Nos. 43517801. Short-term risks assessed using DAT 0-1 residue values.

d Oral doses calculated using formulas presented in the Residential SOPs (February, 2001). Short-term and intermediate-term doses were calculated using the following formulas. Intermediate term doses were each multiplied by the estimated fraction of oxadiazon residue remaining on DAT 7 after application.

Hand-to-mouth oral dose to toddlers on the day of treatment (mg/kg/day) = [application rate (lb ai/acre) x fraction of residue dislodgeable from potentially wet hands (see assumptions) x 11.2 (conversion factor to convert lb ai/acre to μg/cm^2)] x median surface area for 1-3 fingers (20 cm^2/event) x hand-to-mouth rate (ST: 20 events/hour) x exp. time (2 hr/day) x 0.001 mg/µg] / bw (15 kg toddler).

Grass ingestion oral dose to toddlers on the day of treatment (mg/kg/day) = [TTR (μg/cm^2) x ingestion rate of grass (25 cm^2/day) x0.001 mg/µg] / bw (15 kg toddler).

Soil ingestion oral dose to toddlers on the day of treatment (mg/kg/day) = [(application rate (lb ai/acre) x fraction of residue retained on uppermost 1 cm of soil (100% or 1.0/cm) x 4.54E+08 μg/lb conversion factor x 2.47E-08 acre/cm^2 conversion factor x 0.67 cm^3/g soil conversion factor) x 100 mg/day ingestion rate x 1.0E-06 g/μg conversion factor] / bw (15 kg; toddler). Short term dose based residue on the soil on day of application.

NA= Not applicable

Note: TTR - Turf Transferable Residue

4.3.4 Incident Data

Oxadiazon **has not** been reported to cause life-threatening illness or death in humans. Most of the cases appear to be related to irritation to the skin, eyes and mucous membranes. Some cases may be related to an allergic reaction On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, oxadiazon was ranked 192nd with 12 incidents in humans reported and 5 incidents in animals (mostly pets).

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

5.1 DWLOCs[33] for Acute Exposure

An aggregate risk assessment is defined as the evaluation of the likelihood of the occurrence of an adverse health effect resulting from exposure to a single substance via all relevant routes. As part of the aggregate risk assessment, short- and intermediate-term risk assessments require the incorporation of drinking water exposure and the calculation of DWLOC values to estimate the total exposure from all sources. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water that are used to determine how much of the acceptable exposure is available for exposure through drinking water. OPP uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. DWLOC values are not regulatory standards for drinking water; however, they do have regulatory impact through aggregate exposure and risk assessments.

DWLOCs were calculated for oxadiazon based on an oral NOAEL of 12 mg/kg/day from a developmental study, which was selected by HIARC for the short-term (1-7 day) incidental oral exposure (McCarroll, 2001b). An acute RfD was not selected for oxadiazon because there are no food uses (McCarroll, 2001b). However, in accordance with the Updated *Interim Guidance for Incorporating Drinking Water Exposure into Aggregate Risk Assessments* (Stasikowski, 1999), this NOAEL was used to calculate the acute DWLOCs. An uncertainty factor of 100 was applied based on a 10x for intraspecies variation and a 10x for interspecies extrapolation. Therefore, the theoretical acute RfD or the theoretical aPAD[34] would be 0.12 mg/kg/day. The default body weights and daily water consumption values were applied for each target population (*i.e.*, U.S. population, children 1-6, and infants). Default body weights and consumption values for calculation of the DWLOCs were: 2L/70 kg (adult male), 2L/60 kg (adult female) and 1L/10 kg (children and infants), respectively. **Based on a comparison of DWLOCs to the corresponding PRZM/EXAM and SCIGROW values, which show higher values for the DWLOCs, acute exposure to residues of oxadiazon in surface and ground water is not a concern (Table 11a).**

5.2 DWLOCs for Chronic Exposure

A chronic RfD was also not selected by the HIARC because of the lack of food or feed uses (McCarroll, 2001b). Using the line of reasoning developed for the acute DWLOC calculations and put forth in the interim guidance document, a combined chronic/oncogenicity feeding study was selected by HIARC for the dermal and inhalation risk assessments (see Section 3.3). Accordingly, this

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[33] Drinking Water Levels of Comparison

[34] acute Population Adjusted Dose

Table 11a. Summary of Acute DWLOC Calculations for Oxadiazon						
Population Subgroup[1]	Acute Scenario					
	Theoretical aPAD mg/kg/day	Acute Food Exp mg/kg/day	Max Acute Water Exp mg/kg/day[2]	PRZM/EXAM Surface Water EDWC (μg/L)	SCIGROW Ground Water EDWC (μg/L)	Acute DWLOC (μg/L)[3]
U.S. Population	0.12	0.00	0.12	181	0.59	4200
Females 13-50 years old	0.12	0.00	0.12	181	0.59	3600
Infants <1 year old	0.12	0.00	0.12	181	0.59	1200
Children 1-6 years old	0.12	0.00	0.12	181	0.59	1200

[1] Default body weights and consumption values for calculation of the DWLOCs were: 2L/70 kg (adult male), 2L/60 kg (adult female) and 1L/10 kg (child), respectively.

[2] Maximum acute water exposure (mg/kg/day) = [(acute PAD (mg/kg/day) - acute food exposure (mg/kg/day)]

[3] Acute DWLOC(μg/L) = $\frac{\text{[maximum chronic water exposure (mg/kg/day) x body weight (kg)]}}{\text{[water consumption (L) x } 10^{-3} \text{ mg/}\mu\text{g]}}$

NOAEL of 0.36 mg/kg/day, based on adverse liver effects, was used to calculate the chronic DWLOCs ($DWLOC_{chronic}$). An uncertainty factor of 100 was applied (10x for intraspecies and a 10x for interspecies variation). Therefore, the theoretical chronic RfD or the theoretical cPAD[35] would be 0.0036 mg/kg/day. **Residential exposures were not factored into the $DWLOC_{chronic}$ since no long-term residential exposures (handlers or postapplication) are expected**.

As shown in Table 11b, only the adult male and female populations as a whole had DWLOC values that exceeded the surface and ground water targets; consequently, the Agency concludes with reasonable certainty that there is no drinking water risk of concern for these populations exposed to oxadiazon. DWLOCs values derived for infants and children also exceeded the EDWCs for ground water and are, also of no concern to the Agency. On the other hand, the EDWCs for surface water (65 μg/L) based on the Tier II modeling from PRZM/EXAM, were higher than the DWLOCs calculated for infants and children. Since the EDWCs were higher than the chronic values derived for surface and ground water (36 μg/L), the Agency concludes that there is a drinking water risk of concern for infants and children chronically exposed to oxadiazon via drinking water.

5.3 DWLOCs for Cancer

For the cancer (Q_1*) exposure calculations, the Agency used multi-year mean water concentration values. The $DWLOC_{cancer}$ is the concentration in drinking water as a part of the aggregate chronic exposure that results in a negligible cancer risk (10^{-6}).

[35] chronic Population Adjusted Dose

No residential exposures were factored into the equation since no long-term residential exposures (handlers or postapplication) are expected. As shown in Table 11c, EFED's EDWC for

Table 11b. Summary of Chronic DWLOC Calculations for Oxadiazon

Population Subgroup[1]	Chronic Scenario					
	Theoretical cPAD mg/kg/day	Chronic Food Exp mg/kg/day	Max Chronic Water Exp mg/kg/day[2]	PRZM/EXAMS urface Water EDWC ($\mu g/L$)	SCIGROW Ground Water EDWC ($\mu g/L$)	Chronic DWLOC (μg/L)
U.S. Population	0.0036	0.00	0.0036	65	0.59	126
Females 13-50 years old	0.0036	0.00	0.0036	65	0.59	108
Infants <1year old	0.0036	0.00	0.0036	65	0.59	36
Children 1-6 years old	0.0036	0.00	0.0036	65	0.59	36

[1] Default body weights and consumption values for calculation of the DWLOCs were: 2L/70 kg (adult male), 2L/60 kg (adult female) and 1L/10 kg (child), respectively.

[2] Maximum Chronic Water Exposure (mg/kg/day) = [Chronic PAD (mg/kg/day) - Chronic Dietary Exposure (mg/kg/day)]

[3] Chronic DWLOC(μg/L) = $\frac{\text{[maximum chronic water exposure (mg/kg/day) x body weight (kg)]}}{\text{[water consumption (L) x } 10^{-3} \text{ mg/}\mu\text{g]}}$

Table 11c. Summary of Cancer DWLOC Calculations for Oxadiazon

Population	Q*	Negligible Risk Level[1]	Target Max Exposure[2] mg/kg/day	Chronic Food Exposure mg/kg/day	Max Water Exposure[3] mg/kg/day	PRZM/ EXAM SurfaceWater EDWC ($\mu g/L$)	SCIGROW Ground Water EDWC ($\mu g/L$)	Cancer DWLOC[4] (μg/L)
U.S. Pop	7.11e-02	0.000001	0.000014	0.000000	0.00001400	56	0.59	0.490000

[1] $DWLOC_{CANCER}$ was calculated for U.S. population only. Default body weights and consumption values for calculation of the DWLOCs were: 2L/70 kg

[2] Target Maximum Exposure (mg/kg/day) = [negligible risk/Q*]

[3] Maximum Water Exposure (mg/kg/day) = [Target Maximum Exposure - (Chronic Food Exposure + Residential Exposure (Lifetime Average Daily Dose))]

[4] Cancer DWLOC(μg/L) = $\frac{\text{[maximum water exposure (mg/kg/day) x body weight (kg)]}}{\text{[water consumption (L) x } 10^{-3} \text{ mg/}\mu\text{g]}^{2}}$

oxadiazon residues in surface and ground water are higher than the Agency's calculated DWLOCs for the adult U.S. population. **Therefore, the cancer risk exceeds HED's level of concern for lifetime exposure to oxadiazon in drinking water derived from surface and ground water**. It should be noted, however, that EDWC values derived from the SCI-GROW model for the ground water analysis, are based on high concentrations observed in shallow ground water after agricultural treatment of permeable soils. Since this combination of conditions is encountered in only 1% of the agricultural use area in the U.S., it is not likely that oxadiazon would pose a potential cancer concern for exposure to oxadiazon in ground water (Barrett, 1998).

5.4 Aggregrate Risk Assessments

HED did not perform an aggregate risk assessment as part of this reregistration review for oxadiazon because the calculated DWLOC values are based on conservative default values since no monitoring data were available on oxadiazon and the refined model for turf analysis is not completed at this time. In addition, data used to develop residential exposure estimates (dermal exposure values) were also conservative because the highest mean postapplication TTR residue value from the Jazzercize study (MRID No. 43517801) along with the data from the wettable powder formulation instead of the the major formulation (granular) were used. Thus, any aggregation of a conservative water number with a conservative residential exposure estimate would result in an even more conservative expression of aggregate risk. The RARC also noted that guidance from management on this issue is forthcoming.

6.0 CUMULATIVE RISK

FQPA of 1996 stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this reregistration review for oxadiazon because HED has not yet initiated a comprehensive review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of oxadiazon. For purposes of this reregistration decision, EPA has assumed that oxadiazon does not have a common mechanism of toxicity with other substances.

On this basis, the Registrant, Bayer Environmental Science, must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether oxadiazon shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for oxadiazon need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with oxadiazon, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment once the final guidance HED will use for conducting cumulative risk assessments is available.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for

public comment on June 30, 2000 (65 FR 40644-40650) and is available from the OPP Website at: http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-30/6049.pdf . In the draft guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed. The proposed guidance on cumulative risk assessment of pesticide chemicals that have a common mechanism of toxicity is expected to be finalized by the summer of 2001.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

7.0 ENDOCRINE DISRUPTION

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, oxadiazon may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

8.0 DATA NEEDS/LABEL REQUIREMENTS

8.1 Toxicology

28-day Inhalation Study (870.3465)

8.2 Product and Residue Chemistry

Current Confidential Statement of Formula containing nominal concentration, upper limits for all components and lower limits for the a.i.

8.3 Occupational and Residential Exposure

Concurrent Transfer Coefficient measurements along with TTR studies.

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